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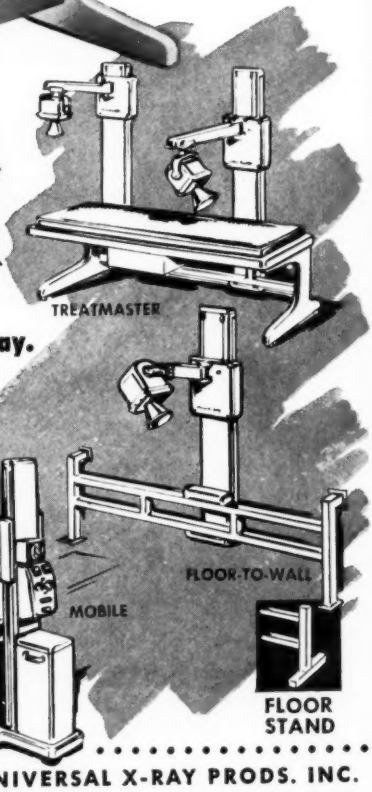

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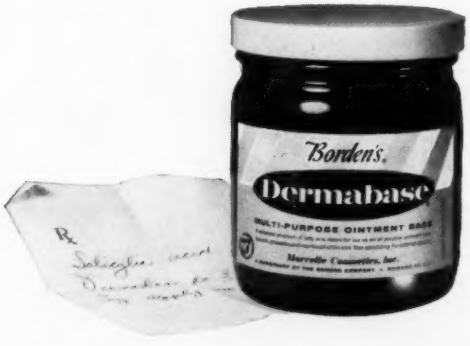

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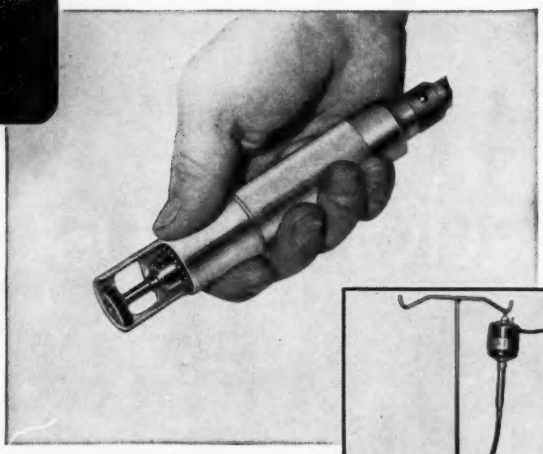

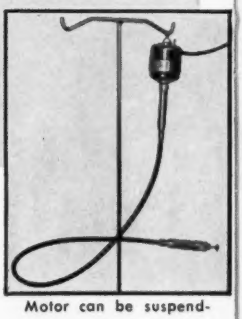

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Use of Banthīne is described[1] in Wiener's recent text: "The main indication for dermatologic use is hyperhidrosis, but it has also been found useful in the control of normal sweating, in dyshidrotic vesicular eruptions, in intertrigo, in contact dermatitis, and in suppurative hydradenitis axillaris. The average initial adult dose is 50 mg. administered orally or parenterally. More or less may be given three times daily, but the daily total should not exceed 450 mg. The daily dosage in the treatment of hyperhidrosis is 100 to 200 mg., but higher doses may be necessary. . . . Following a dose of 100 mg., dryness of the palms usually sets in after thirty to forty-five minutes and lasts four to five hours. . . . The clinical reports have so far been favorable."

Banthīne is also recommended[3] for the hyperhidrosis occurring with *Tinea pedis*.

1. Wiener, K.: Systemic Associations and Treatment of Skin Diseases, St. Louis, The C. V. Mosby Company, 1955, pp. 329; 458-459.
2. Perry, D. J.; Mount, G. D., and Browne, B. W.: The Effect of Varying Oral Dosages of Banthīne, Pro-Banthīne and Prantal on the Galvanic Skin Response, J. Invest. Dermat. *28*:239 (March) 1957.
3. Olansky, S., and Callaway, J. L., in Modern Medicine 1958 Annual (Part 1): Management of Superficial Infections, Minneapolis, Modern Medicine, 1957, p. 46.

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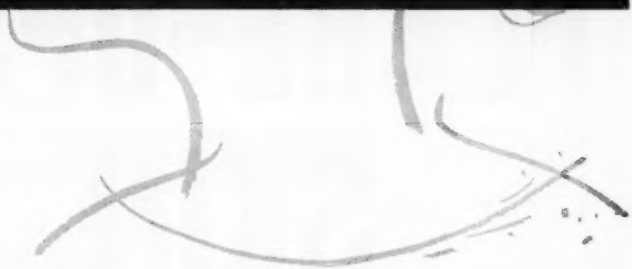

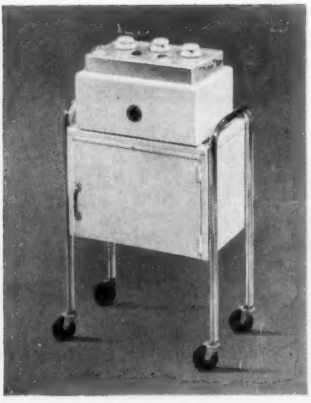

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References: 1. Sokoloff, O. J.: Meprobamate (Miltown) as adjunct in treatment of anogenital pruritus. A.M.A. Arch. Dermat. **74**:393, Oct. 1956. 2. LeVan, P.: Clinical dermatologic studies of four chemically different tranquilizers. Clinical Med. **4**:1089, Sept. 1957.

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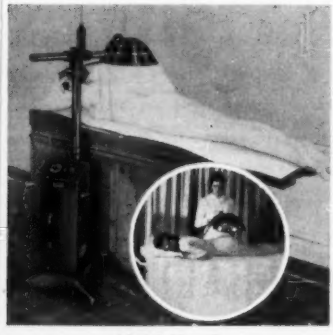

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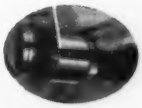

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1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

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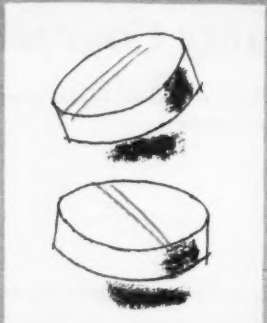

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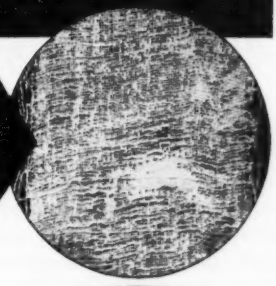

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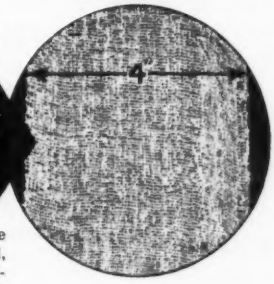

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Kenalog in ointment, cream or lotion form may be used for treatment of a wide variety of dermatoses including:

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In double-blind tests in 309 patients comparing 0.1% Kenalog and 1.0% hydrocortisone, Kenalog exhibited superior anti-inflammatory, antiallergic and antipruritic activity.

Investigator	Total Cases	Kenalog Superior	Hydrocortisone Superior	Neither Effective	Equally Effective
Goodman[3]	50	32	3		15
Smith et al.[4]	109	75	3	3	28
Fitzpatrick et al.[5]	120	61	5		54
Lerner[6]	30	20	4	1	5
	309	188	15	4	102

Kenalog is extremely well tolerated locally. No systemic toxicity has been observed in clinical studies, published and in progress, involving over 1,000 patients.[1,3] Metabolic studies show that there is no electrolyte disturbance when Kenalog is applied topically.[1,4,5]

1. Reports to the Squibb Institute for Medical Research.
2. Howell, C. M.: Squibb Clinical Research Notes 1:5 (Oct.) 1958.
3. Goodman, J. J.: Ibid. p. 1.
4. Smith, J. G.; Zawisza, R. J., and Blank, H.: Ibid. p. 6.
5. Fitzpatrick, T.; Crowe, F. W., and Walker, S. A.: Ibid. p. 12.
6. Lerner, A. B.: Ibid. p. 2.
7. Robinson, R. C. V.: Bull. School of Med., U. Maryland 43:54 (July) 1958.

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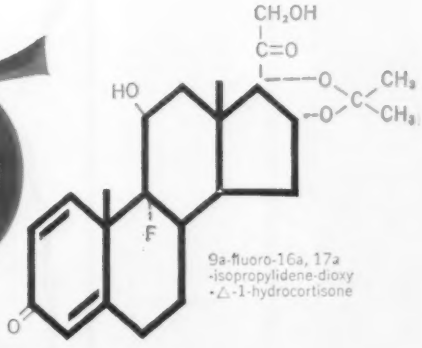

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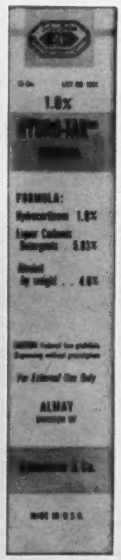

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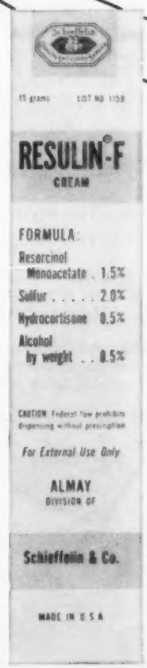

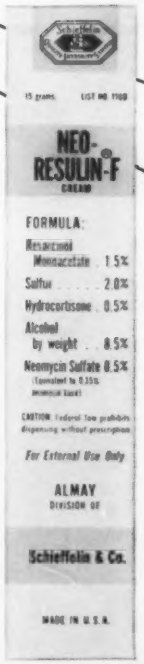

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*Peck, S. M.; Traub, E. F., and Spoor, H. J.: A.M.A. Arch. Derm. & Syph. 67:263, 1953.

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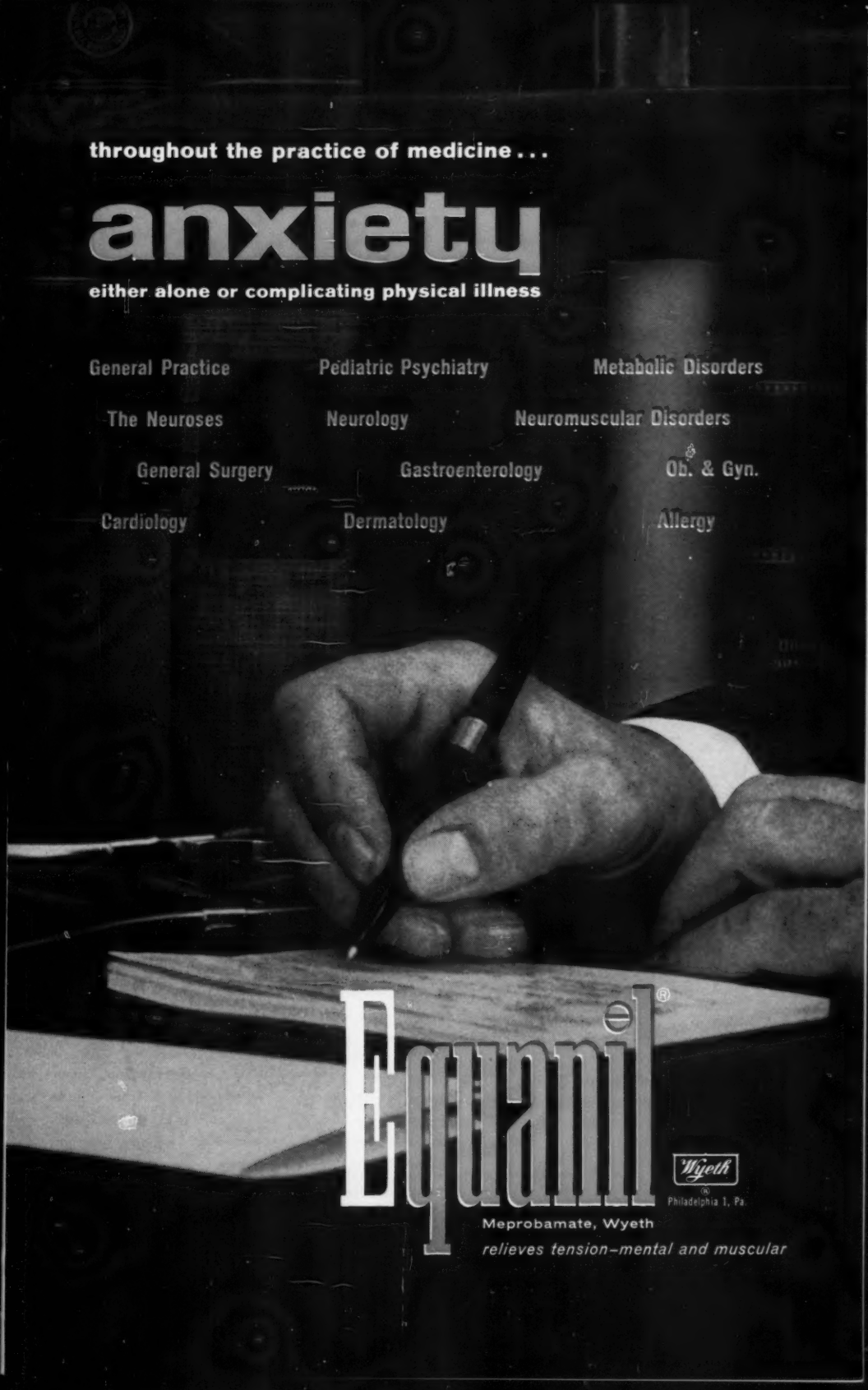
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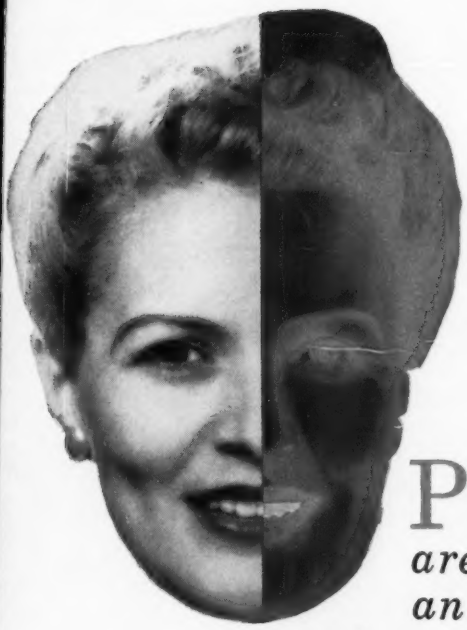

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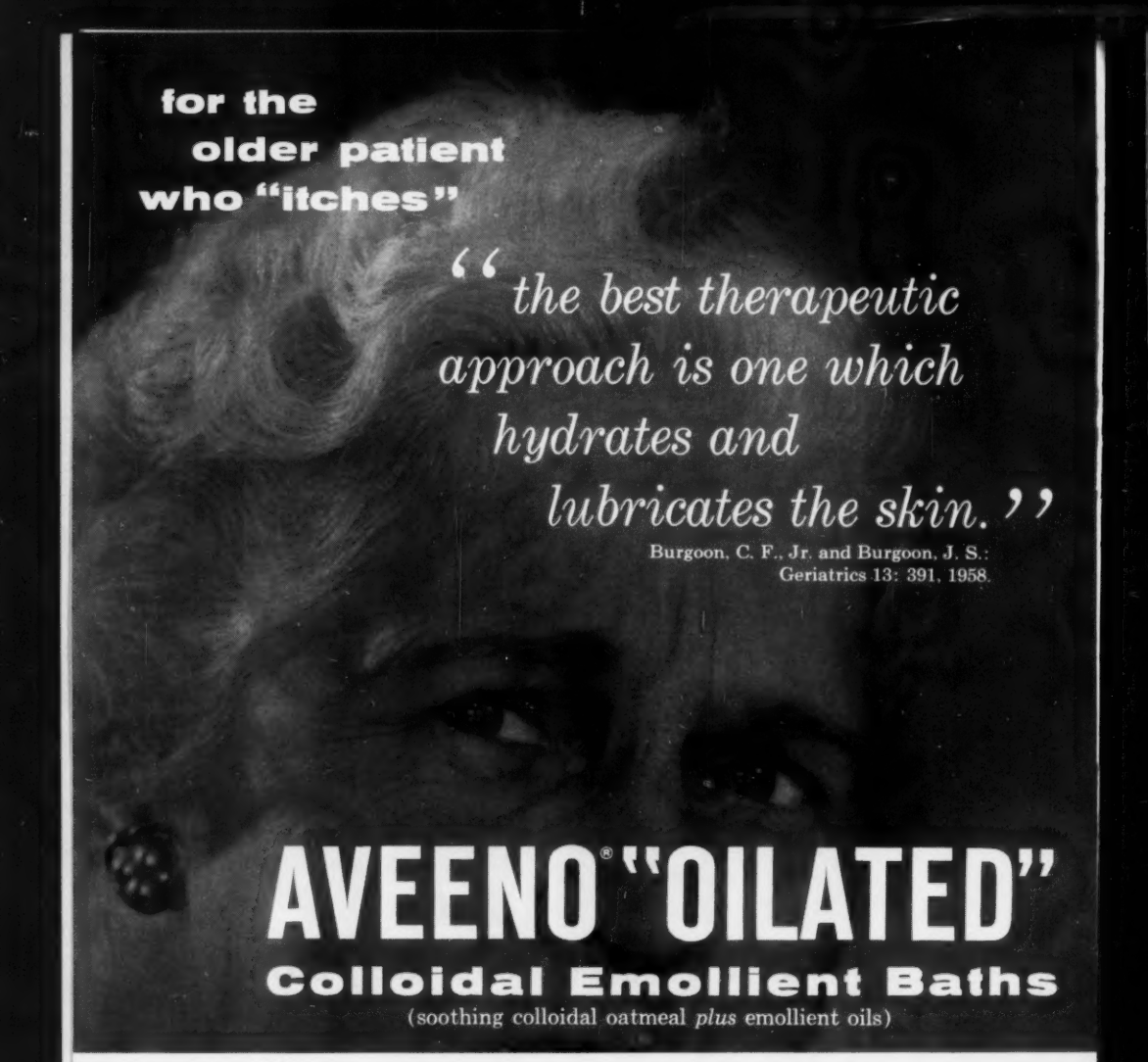
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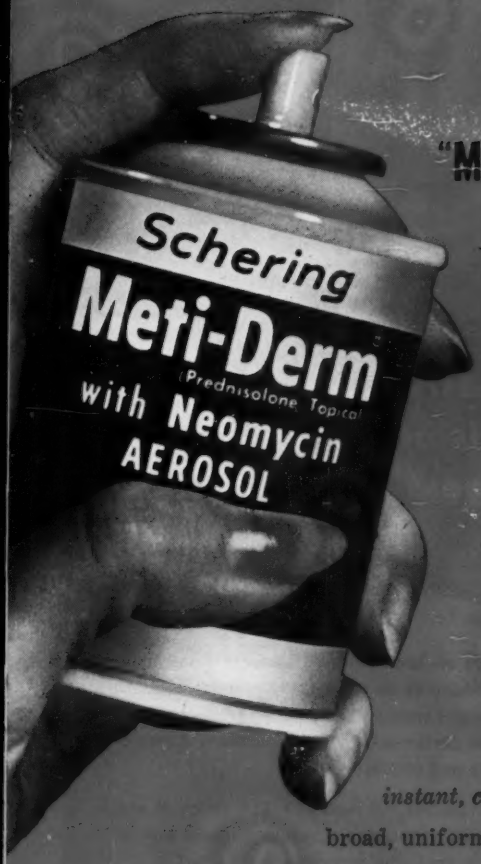

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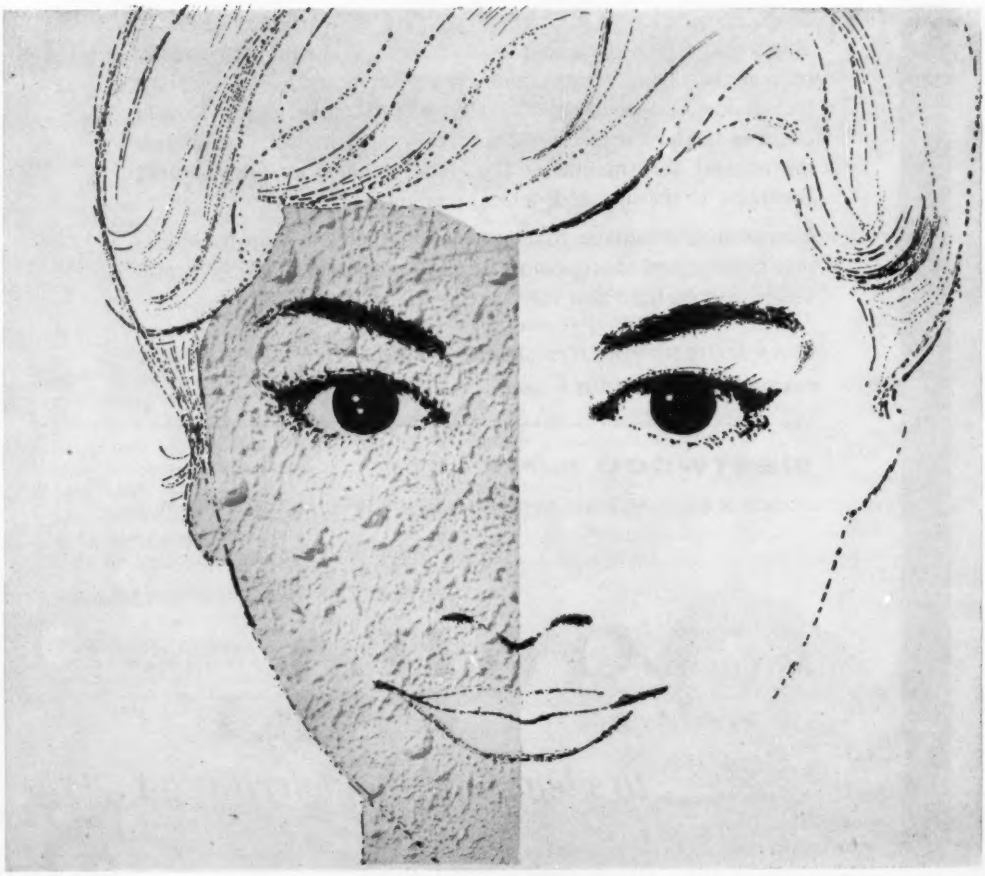

A.M.A. ARCHIVES OF
DERMATOLOGY

Does the Rosacea-like Tuberculid Exist?

HENRY E. MICHELSON, M.D., Minneapolis

A euphonious term like "rosacea-like tuberculid of Lewandowsky" is so pleasing to the ear that it comes instantaneously to the mind when dermatologists see a patient who has a variety of papular lesions on his face, lesions which resemble rosacea, or which at least appear in those areas where rosacea usually occurs. Having committed themselves to the diagnosis of "Lewandowsky's disease," they naturally must defend their diagnosis; consequently, the monotonous debate concerning the positive diascopy of the lesion, its color, and the presence of tuberculoid structure of a type similar to a lupus nodule is again indulged in. The fact that bacillary evidence is lacking, that the tuberculin reactions are negative, that there is no evidence of active, internal tuberculosis, and, most important, that the patient is entirely well and socially and economically capable does not change the self-satisfying diagnosis. These negative findings are completely ignored, because the topography and the morphology of the lesion have impressed the diagnostician.

It is of both academic and medical importance that we again attempt to review the subject; for, despite articles published by me and my co-workers, especially Laymon, in which the rarity of the true micropapular tuberculid of the face was pointed out and in which it was emphasized that, in our opinion, most of the cases presented before dermatological societies might well be examples of lupoid rosacea, this latter diagnosis is seldom the one presented. This view is by no means confined to us, as articles by Miescher, Snapp, and others attest.

A painstaking inspection of continental dermatological society transactions, as published in the *Zentralblatt, Hautarzt, Zeitschrift für Dermatologie*, et cetera, reveals that "rosacea-like tuberculid" is a diagnosis which fascinates dermatologists over the world; the morphology of the lesion is more impressive to them than is the lack of proof of an existing tuberculosis.

If one analyzes the term "rosacea-like tuberculid," one first must define a tuberculid—no easy task—and then must try to decide whether the variety in question fulfills the well-defined criteria of diagnosis.

An "id" eruption is looked upon as a more or less widely distributed, but localized, reaction in the skin, which is brought about by a rapid dissemination of a causative agent coming from an identified and demonstrable focus. A vigorous ability to react to this agent is an admitted propensity of the body; it is translated as a high degree of allergy. However, the term may be loosely used. For example, a general papular eruption, associated with a kerion, may be called a trichophytid. In this instance, both the focus and the reaction are in harmony with the definition of the term. However, a syphilid

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Professor of Dermatology Emeritus from the Division of Dermatology, University of Minnesota (Francis W. Lynch, M.D., Director).

may be any of the early cutaneous lesions of syphilis, without a focus. The term may have originated when the chancre was looked upon as the focus instead of the reaction at the port of entry of the spirochetes. A trichophytid is due to spores or fungi. A syphilid is caused by a reaction to spirochetes.

The origin of the term "tuberculid" is different. In the long battle to establish the entity of lupus vulgaris, the question of the form of tuberculous reaction in the skin different from that found in a lymph node or lung had to be debated and resolved. Thus, the pathology of tuberculosis of the skin was recognized, and the pathologic changes found in lupus vulgaris, with its lack of caseation, were accepted as the standard. However, other skin lesions, which were thought to be tuberculous in origin, were known to exist. These lesions differed histologically from lupus vulgaris, and it was therefore proposed by Boeck, Krebich, Darier, and others that there was a "pseudotuberculosis" of the skin, possibly caused by the toxin, tuberculin. To this group of clinically-recognized lesions the term "tuberculid" was applied. Gradually, various types were added, and they all constituted a group which had somewhat similar characteristics.

Darier's concept of the tuberculids was a broad one, which admitted the existence of tuberculous lesions of low virulence, containing very few, if any, demonstrable bacilli and having an anatomical structure which varied from the accepted classical form of cutaneous tuberculosis as exemplified by lupus vulgaris.

Gradually, because of the work of Darier, Neisser, Jadassohn, and Pautrier, it was accepted that tuberculosis could produce a great variety of morphologic lesions on the skin, some being more or less chronic in their properties, while others were atypical. In this latter category were placed the tuberculids, and the term became the designation for various cutaneous lesions which had been brought about by degrees of tissue reaction against hematogenously sown bacilli. The lesions varied in size, form, and character. Some were lichenoid; others were papular, and they could manifest scaling, pustulation, or even ulceration. Their life history was relatively short, and, because of some destruction, there was often scarring. Thus it can readily be seen that the term "tuberculid" is so inclusive that diagnostic criteria scarcely exist, either macroscopically or microscopically.

The association of other forms of tuberculosis with tuberculids had long been known, as, for example, the association of lymph-node tuberculosis with lichen scrofulosum or with erythema induratum. Therefore, the idea of a focus being necessary in order to provide the causative organism became established. Today the term tuberculid implies an extracutaneous source, bacillary implantations, and a localized tissue reaction.

What cutaneous lesions to include under the term also became a problem. For example, was lupus miliaris disseminatus faciei a tuberculid? Or, could a clinical lesion of granuloma anulare, which had tuberculoid structure, be a tuberculid?

It may be seen that, even today, strict boundary lines cannot be drawn, and that, in general, tuberculids are lesions which do not progress very much from their inceptive form, which do not grow by continuity, and which heal after the local destruction has been overcome.

Tuberculids, especially of the so-called necrotic, papular variety, occurred on fairly fixed, anatomic locations, and among those was the face.

Lewandowsky in 1917 described the condition we are discussing. He designated a papular eruption, occurring on the face, as a rosacea-like tuberculid because he thought that the individual lesions had the characteristics of papular tuberculids and because they were found in tissue which has a predilection for rosacea.

I have mentioned how difficult it is to define tuberculid lesions. So, also, rosacea is a decidedly variable condition. The lesions may be tiny papules or fairly large papules.

They may occur in normal skin or in areas of telangiectasia. They may lie in the skin or be slightly elevated. There may be only a few, widely scattered lesions, or they may be closely studded together, forming a contiguous mass. The contour of the skin may be normal, or when there are numerous lesions there may be considerable edema. Thus, one may say that there are no morphologic criteria diagnostic of rosacea.

Microscopically the problem is just as intricate. There is no criterion upon which the microscopic diagnosis of tuberculid can be made. Some tuberculoid structure must be present; if it were not, the diagnosis of tuberculid would not be considered. However, neither in form nor in other fine points does the tuberculid differ from mere tuberculoid structure. Its diagnosis depends upon combining the clinical features of the lesion with its histologic changes.

The diagnosis of rosacea-like tuberculid, therefore, does not depend upon morphology or microscopy but is arrived at because the lesion, which has tuberculoid structure, occurs in or on the face, in areas where rosacea may occur—not because it looks like ordinary rosacea, but because it occupies the same areas!

Having decided that the case is one of rosacea-like tuberculid, the presenter of the case then is confronted with proving that the "tuberculid" is tuberculous. How? The usual approach is hurriedly made. Stains for bacilli in the sections are invariably negative. The tuberculin reaction may or may not be positive. This depends upon many factors, and, if it is positive, does not prove the lesion to be tuberculous. Examinations of the chest and gland-bearing areas may yield evidence of value. Animal inoculations have been negative in most of the cases reported. Thus, the presenter may be confronted with a decision between retracting his diagnosis or adhering to the diagnosis of tuberculid in spite of the fact that no tuberculosis can be either suspected or proven.

He may state that the histologic findings hint at tuberculosis and that if it is not tuberculous then what is it? The answer from my point of view would be lupoid rosacea.

Doubt concerning the existence of rosacea-like tuberculid has been expressed before many dermatological societies. For example, F. Sommer,[1] at the Congress of the German Dermatological Society held in Hamburg in 1948, presented a patient with the diagnosis of rosacea lupoides. This 34-year-old woman had livid plaques on the cheeks, in which there were numerous yellowish-brown small papules which, under glass pressure, had the appearance of apple jelly. There were also some pustules. Histologic examination revealed, among other findings, areas of tuberculoid structure. There was no proof of the presence of systemic tuberculosis.

The case provoked considerable discussion. Moncorps thought that the diagnosis rested between rosacea and lupus miliaris faciei, but remarked that the necrosis found in the latter condition was absent. Miescher, who has shown great interest in this intriguing problem, in his usual learned way, called attention to Lewandowsky's first description of a rosacea-like eruption with interspersed nodules, which were positive under diascopic pressure and histologically were small, tuberculoid granulomas. He further emphasized that histological analysis of many cases of rosacea revealed that there was no sharp boundary between some forms of rosacea and the tuberculids of the face. He also stated that deeper excisions often showed tuberculoid granulomas in the subcutis that could not be demonstrated clinically. He proposed the view that the nodules found in tissue already altered by rosacea might be microbids, but he was not yet convinced about the etiology. His animal experiments gave results negative for tuberculosis. Jordan stated that in such cases as the one presented one need only consider rosacea-like tuberculid and lupoid rosacea. He upheld Miescher's views and reemphasized the frequency with which tuberculoid structure was found in ordinary rosacea. He

also doubted if a true or real rosacea-like tuberculid existed.

Eight years later, at the Vienna meeting of the German Dermatological Society (1956), G. Ehrmann demonstrated a 35-year-old man under the diagnosis of lupus follicularis disseminatus faciei.[2] The eruption consisted of small papules, occurring in the central portions of the face, which were brown and which were diagnosed histologically as "Kaposi acne." A search for systemic tuberculosis yielded negative results. Treatment with isoniazid (Rimifon) (antituberculosis drug) and Grenz rays was not successful. The tuberculin reaction was negative.

Sixteen members of the Society entered the discussion, but I shall not quote all of the opinions expressed. Gottron, whose experience with cutaneous tuberculosis is impressive, stated, in part, that lupus miliaris faciei lesions did not appear in erythematous areas. This caused him to favor a diagnosis of lupoid rosacea, rather than the presenting diagnosis. G. Riehl mentioned that ordinary treatment for rosacea was effective only in cases that actually were rosacea and not in cases of rosacea-like tuberculid. O. Braun-Falco called attention to the fact that isoniazid (INH) therapy is not specific and should not be used as a diagnostic criterion.

A. Wiedmann expressed a view which impressed me, namely, that when one seeks to make a differential diagnosis *ex juvantibus* in such cases, one is on very uncertain ground. Neither the morphology nor the histology nor even animal inoculations can give conclusive evidence. We have no known method today which allows certain differential deductions. Miescher was also present at this meeting, and he stated that a clear differentiation between lupus miliaris faciei, rosacea-like tuberculid, and micronodular rosacea (note the term!) is not only clinically, but also histologically, uncertain. Transitional forms exist: For example, a case which is clinically lupus miliaris faciei may not have the classic microscopic findings, with the caseating granuloma, but may show merely a collection of epithelioid cells, with or without the halo of lymphocytes which is characteristic of rosacea-like tuberculid. On the other hand, in typical cases of micronodular rosacea, often a collection of lymphocytes with a central area of epithelioid cells is found.

Thus one notes that leaders in the German Dermatological Society realize the difficulty of the problem and that they do not believe that differentiation between certain forms of rosacea and types of facial tuberculids is possible with the methods that we possess as this time.

American dermatologists, because of their relatively small experience with cutaneous tuberculosis, seem to have more certain views, especially about the morphology of rosacea-like tuberculid. For example, a 34-year old woman was presented by the University Hospital Staff before the Detroit Dermatological Society meeting held in Ann Arbor, Mich., on March 13, 1957, under the diagnosis of rosacea-like tuberculid of Lewandowsky. The eruption had been present for four years and consisted of apple-jelly nodules in areas of erythema on the cheeks and bridge of the nose. Findings for tuberculosis were negative, except for a positive skin test to O. T. 1:10,000. Treatment had been with isoniazid. Histologically, there were epithelioid foci suggestive of young tubercles, thus supporting the diagnosis of a tuberculid.

Blumenthal, whose experience with cutaneous tuberculosis is large, expressed views which are in accord with those of continental dermatologists. He stated that it is very difficult to classify an individual case as tuberculosis or tuberculid. He thought this particular case, as a whole, gave the picture of rosacea-like tuberculid, but some lesions were those of lupus miliaris faciei. He emphasized the resistance of such cases to antibiotics and antituberculosis drugs but stated that self-healing was a common tendency. He brought out the occurrence of combinations of lesions which had one or another characteristic. Butler stated that he had treated this same patient over a long period, and he expressed

astonishment at the resistance to the various antituberculosis remedies that he had tried. Curtis said he was reluctant to use steroids, which a member of the Society suggested, but he thought streptomycin and isoniazid should be used.[3]

Catinella, at the Atlantic Dermatological Conference, held in Boston on March 23, 1957, presented a 36-year-old female patient with the diagnosis of rosacea-like tuberculid (micropapular tuberculid). The eruption had been present for one year, and there had been partial remissions followed by exacerbations. The lesions were small red or brown papules and nodules, some covered with scales; others bore crusts. The tuberculin reaction was positive, but all other searches for tuberculosis were negative. Biopsy specimens showed discrete and confluent epithelioid tubercles without caseation necrosis, but there was a thick surrounding wall of lymphocytes.[4]

The discussion by five members expressed the same uncertainty that one encounters in most of the reports. The presenter stated in part that the reason for classifying the case as rosacea-like tuberculid or as micropapular tuberculid was merely that it fitted what had previously been considered the classical description of the disease.

This I consider worthy of comment, for I find that it is very difficult to decide what "the classical description" of the disease is. I have encountered a number of other case presentations, largely before continental dermatological societies, but the above quotations are representative of the mixed feelings that members express about the problem.

There have been only a few special articles in the literature on the subject of rosacea-like tuberculid, and none in the last few years. I shall not review the past literature, for it is readily available to those interested. Of the more recent literature on the subject, the article by Lissia[5] is of interest. This communication was presented before the Italian Dermatological Society on April 25, 1954.

The author discussed the clinicomorphological characteristics of the condition. He thought that the results of culture allowed him to exclude pyogenic infections, and he readily excluded the usual diseases considered in differential diagnosis, but the exclusion of lupus miliaris faciei he found more difficult. He also pointed out that if there were a reactivation of the process under isoniazid therapy this fact spoke in favor of the tuberculous etiology. Lissia does not discuss the difficulty of excluding lupoid rosacea, but he does bring out many immunologic and biologic facts concerning the pathogenesis of tuberculids.

As already mentioned, an important point in this discussion is to evaluate, if possible, the meaning and use of the term tuberculid.

Does a division of tuberculosis of the skin and tuberculids exist? And if it does, what are the criteria for differentiation? This subject was ably discussed by Bolgert and Lévy.[6] They insist that there is no fundamental difference between the so-called true tuberculoderms and the dermic tuberculids. They note that bacilli are rare or absent in both groups, admitting that there is a greater degree of bacillary negativity in the tuberculids. However, bacterial identification, even though highly desirable, is of little practical value because of the uncertainty of our present-day methods, regardless of the clinical grouping. They mention that anatomical considerations do not allow a clear-cut distinction, for so-called typical tuberculous structure is often rudimentary, even in types such as lupus vulgaris or tuberculosis verrucosa cutis, which are universally considered to be tuberculous in origin. Certainly, microscopic examinations do not permit one to state that there is a distinct histologic form of tuberculosis which should be called a tuberculid reaction. Tuberculoid structure must be present before tuberculosis may even be considered as the cause of a pathologic reaction in a case under consideration. Also, every experienced histologist realizes the difficulty encountered in pronouncing a specific cause for tuberculoid structure.

Therefore, one must conclude that tuberculosis cutis and tuberculid cannot be separated on an anatomical basis.

These authors further admit that tuberculin sensitivity is an aid in diagnosing all forms of tuberculosis, but it is positive in almost all forms of cutaneous tuberculosis; thus it is not of specific value in the differentiation of types.

In spite of the fact that there is much in common in tuberculosis cutis and tuberculids, one must state that there is a very marked difference pathogenically and morphologically. Usage has established the term "tuberculid," and efforts to substitute a more accurate term, such as "tuberculosis papulonecrotica," have not received universal acceptance. Gans, in the first edition of his book on histopathology, proposed a classification of cutaneous tuberculosis in which he eliminated the term tuberculid, but the nomenclature he proposed is rarely used when cases are presented before dermatological societies the world over.

One must conclude, then, that the term "tuberculid" has a special meaning for dermatologists and that it is based on a concept of the pathogenesis, evolution, and morphology of a certain group of lesions. It is assumed that the lesions result from a vigorous local reaction to hematogenously-implanted tubercle bacilli in a subject whose skin has a high degree of resistance to tuberculous infection and that, because of the accompanying allergy, the lesions are successfully localized, have certain characteristics, and are more or less self-healing.

I do not believe that dermatologists, in using the term "tuberculid," attach to it any particular form of bacillary disintegration, special cellular reaction, or, above all, toxic —not bacillary—origin. I furthermore do not believe that they associate the presence of tuberculid lesions with active systemic tuberculosis, although they should search for the presence of a demonstrable or occult focus when they use the term. Even though patients who exhibit tuberculids usually do not show evidence of severe tuberculosis, it cannot be stated that all patients with tuberculids have a high degree of resistance to tuberculosis. In my own experience I have seen patients die of pulmonary tuberculosis who had previous, and even simultaneous, outbursts of necrotic, papular tuberculids.

How, then, may what has been said apply to the disease in question? Is the so-called rosacea-like tuberculid a particular form of tuberculosis, aside from its morphologic changes? Or may it be grouped with the papular tuberculids and therefore be appraised in much the same manner that tuberculids are when they occur in other parts of the body?

Each distinct form of tuberculid has certain well-established characteristics. Thus, lichen scrofulosorum has lichenoid lesions, usually appearing on the trunk, often associated with tuberculous adenitis, and occurring almost exclusively in children. Erythema induratum is found on the lower legs, occurs more commonly in females, tends to seasonal recurrence, etc. But the necrotic, papular tuberculid varies as to size and areas of location and tends to have different characteristics in different locations. The lesions may be minute hard papules, or they may be fairly large soft nodules. They may remain as papules until they regress, or they may necrose, ulcerate, and slough, leaving a scar. In any event, they represent the well-known cycle of the pathologic changes of tuberculosis. If the lesions occur on the face, and if they are of fair size, they represent what historically was known as acnitis. If the lesions are small, with little visible retrogressive change, they are termed micropapular or micronodular tuberculids.

But if these small lesions occur in erythematous or telangiectatic areas, and if the over-all picture is suggestive of rosacea, the term "rosacea-like tuberculid" is used. In this connection, it must be stressed that the lesion essential for such a diagnosis must be one that is consistent with a form of tuberculid and not merely a lesion with an erythematous base, occurring in a special

location, but it must be a papule, of varying size, density, color, etc. If, then, the excised lesion shows distinct tuberculoid structure, which predominates the reaction, and if there is other corroborative evidence for tuberculosis, one cannot find fault with the diagnosis of rosacea-like tuberculid, even though he may not like the term.

Resistance to the diagnosis arises when the diagnosis is made with a frequency that is out of all proportion to the number of patients, with other forms of tuberculids, that are observed, for example, in a geographic locality for which there is a more or less fixed ratio of the number of cases of tuberculosis cutis which may be expected in a given period of time. When very few patients with papular tuberculids are presumably encountered in such a locality, and the number of patients presented under the diagnosis of rosacea-like tuberculid increases, it is difficult to believe that, for some unaccountable reason, tuberculosis cutis, in the form of a facial tuberculid, has increased in incidence in that particular locality. This is especially true when one realizes that all other forms of cutaneous tuberculosis have disappeared in that locality almost to the vanishing point (which is consistent with the general control of infectious tuberculosis).

One then must question this specific diagnosis and emphasize that another cutaneous condition may show a similar morphologic and histologic pattern. Such a condition is papular, nodular, or lupoid rosacea. To be sure, one cannot make this diagnosis on a basis of ratio alone, but the frequency of rosacea compared with the paucity of tuberculoderms should certainly be impressive. In spite of this, differential diagnosis is necessary, and, as stated before, such a differential diagnosis may be very difficult. It must be reiterated that neither rosacea-like tuberculid nor small papular tuberculid nor papular or mixed forms of rosacea have indubitable characteristics.

The history of the disease is of great importance. Patients who have rosacea usually relate a long history of "complexion trouble," the onset of which was slow and the development gradual, with periods of exacerbation and regression. The condition becomes worse with each succeeding outburst.

Rosacea occurs more commonly in middle-aged persons who often state that they had acne vulgaris in their younger years. Stokes and others have attributed to rosacea patients personality and vascular characteristics which are valuable in assaying a case.

Tuberculid eruptions often begin with a rather sudden outburst, sometimes called a "shower." The lesions are generally of the same age, and the individual lesions are alike as to size and character. They reach their maturity in a rather short time and then remain in situ, or they may regress. Recurrences of necrotic papular tuberculids on the olecranon or knee areas are common, but there is usually a long period, even years, between attacks of the disease. Facial tuberculids, for some unknown reason, are not apt to recur. The individual lesion has no definite fixed properties, but some characteristics pertain for lesions occurring in certain body areas. For example, papular tuberculids occurring on the toes or fingers are small and have the appearance of a small clavus with a dark red or blue surrounding inflammatory zone. Lesions occurring at the elbows are often pustular, while those on the lower leg may be topped with dark, almost black crusts. Tuberculids on the face vary in size, are almost always of a yellowish-red or brown color, are soft and smooth, and resemble an individual lupus vulgaris nodule.

The microscopic anatomy consists of two kinds of inflammation. The superficial central portion is banal and necrotic, while the lower peripheral portion shows tuberculoid structure, often in the form of well-formed but not caseating tubercles. There may be, and often is, a fair degree of lymphocytic infiltrate about the entire papule, but the immediately adjacent tissue is free from reaction. Elastic tissue stains reveal a com-

plete destruction of the elastic fibers in the central portion, but the elastic fiber outlines of blood vessels can usually be found.

The lesions are not necessarily follicular; in fact, often they are not follicular. In lesions of papular rosacea the reaction frequently is found around the sebaceous apparatus; often remnants of sebaceous glands can easily be identified. The reaction in this locale may even have some of the characteristics of the phagocytic stage of steatonecrosis. The tuberculoid structure found here may well be a foreign-body reaction against the disintegrating sebaceous (fat) cells. In lupoid rosacea a pure epithelioid reaction is rare and complete tubercle formation is not anticipated.

In spite of the quoted differences, there is always an element of doubt in a differential microscopic diagnosis.

Lupus miliaris faciei may be diagnosed clinically with a high degree of accuracy. The localization on the eyelids, the upper lip, and the chin; the sharply outlined, small, lozenge-shaped papule; the completely normal surrounding tissues, and the central softening of the lesion are evidence favoring the diagnosis. The classical microscopic picture is that of a sharply outlined, small mass of tuberculoid reaction, tubercle-like in aspect, with or without strong central necrosis. The condition occurs most commonly in young adult males. It almost never recurs, and it is self-healing in about 12 to 18 months' time. The cause of lupus miliaris faciei has not been established, in spite of the classification with tuberculoderms. Lesions which meet the foregoing description may be found, interspersed with other papular lesions, in both micronodular tuberculids and lupoid rosacea, but in a well-authenticated case of lupus miliaris faciei the eruption is monomorphous.

The differential diagnoses of these conditions cannot be described further. It can only be stated that all patients who have papular lesions on the face which resemble any of the above-described diseases require careful, slow, deliberative study and that a final diagnosis should be delayed until all the evidence is evaluated; furthermore, a period of observation, even with therapeutic trials, is advisable.

On a percentage basis, one should give the diagnosis of "lupoid rosacea" priority, especially in a middle-aged female patient. Tuberculosis as a cause of this condition, or even implied in a diagnostic term, should not be utilized until a definite proof of tuberculosis has been established. The far-reaching psychological effects of a diagnosis of the presence of tuberculosis are too great, not only on the patient but on his family, to be entered into without deep thought.

I am convinced, from my own experience and from a review of the literature on reported cases, as well as from those cases of cutaneous tuberculosis recently reported, that papular tuberculids of the face rarely occur and, furthermore, that the micropapular type of lesion, which may occur in patients whose eruption has an over-all appearance of rosacea, is extremely rare. The knowledge concerning lupoid rosacea is not complete; certainly it is not final. In fact, there is much yet to be known about any type of rosacea.

In conclusion, one might state that the possibility of rosacea-like tuberculid exists, but an assay of the literature and a review of one's own experience impresses one with the extreme rarity of well-authenticated cases which meet the rigid requirements for the diagnosis.

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A Localized Outbreak in New York of Tinea Capitis Due to Trichophyton Violaceum

Observations with Special Reference to Mixed Infections of the Scalp

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Infection of the scalp with Trichophyton violaceum is a rare finding in the United States, although it is common in other areas of the world.[1-3] At the Skin and Cancer Unit of University Hospital, New York, there have been eight cases of tinea capitis due to T. violaceum from 1946 through 1957 (seven cases reported before 1956[4] and one since). Other sporadic cases of scalp infection with this organism have been reported.[5,6]

The observation of two species of fungi simultaneously infecting the same scalp is rare. Muskatblit[7] has reviewed the earlier literature on this subject and reported his own case of a combined scalp infection with T. schoenleini and T. violaceum. Other reports describe mixed infections of the scalp with Microsporum audouini and M. canis,[8] T. schoenleini and T. violaceum,[9] T. violaceum and T. tonsurans,[2,10] and T. granulosum and T. violaceum.[11]

The purpose of this paper is to report on a localized outbreak of tinea capitis due to T. violaceum, with observations on mixed fungous infections of the scalp. Brief mention of this outbreak has already been made by Hazen et al.,[12] who have also noted mixed scalp infections with T. violaceum and M. audouini and also with T. violaceum and M. canis.

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Method

All patients of a state school* for mentally retarded persons were examined by staff physicians for clinical evidence of tinea capitis. Those with positive clinical signs were referred to us for further examination and included 88 patients from 5 to 17 years of age. They were examined under regular artificial light and under Wood's light. Both greenish fluorescent hairs and nonfluorescent hairs from clinically involved areas of the scalp were plucked, cultured on Sabouraud's agar and Sabouraud-antibiotic agar,[13] and examined microscopically, both in NaOH preparations and after staining by the Hotchkiss-McManus technique. Cultures were incubated at room temperature and examined periodically, being discarded as negative only after incubation for four weeks. Two or more mycologic examinations were done on many of the subjects.

Results

Clinical Observations.—In the subjects infected only with T. violaceum the most prominent sign of infection was the presence of grayish-white, somewhat adherent scales, which occurred in irregularly contoured patches. The hairs were relatively sparser in these areas but not necessarily broken off. A few scalps exhibited mild superficial folliculitis with pyogenic infection. "Black dots" were seen in only a single instance.

It is important to note that the majority of clinically screened cases in this series were not typical in appearance for tinea capitis and that the prevalence of trichotillomania, pyoderma, and eczematoid dermatitis in these institutionalized patients

* Harold H. Berman, Director of the Willowbrook State School, Staten Island, N. Y., cooperated in making this study possible.

made differential diagnosis difficult on clinical grounds alone.

Mycologic Studies.—Of the 88 subjects who showed clinical signs of tinea capitis, 44 (50%) yielded cultures of T. violaceum, either alone or in combination with other fungi. In three additional subjects microscopic examination of hairs showed large spored endothrix fungi but no cultures were obtained. Cultures of M. audouini and/or M. canis were isolated from 27 subjects (30%), while 17 (20%) were culturally negative.

Results of Cultural Examination of Hairs from Eighty-Eight Subjects with Clinical Evidence of Tinea Capitis

Culture	Subjects, No.
Single infection of the scalp	
T. violaceum	16
M. audouini	14
M. canis	8
Double infection of the scalp	
T. violaceum & M. audouini	12
T. violaceum & M. canis	12
M. audouini & M. canis	5
Triple infection of the scalp	
T. violaceum, M. audouini, & M. canis	4
No culture obtained	17
	88

A large number of mixed infections were encountered (Table), including infections with T. violaceum and a Microsporum or with two species of Microsporum. In addition, from each of four subjects, cultures of T. violaceum, M. canis, and M. audouini were obtained. In three of the four cases, all three fungi were isolated from hairs taken at the same time. From the fourth case, T. violaceum was isolated at first; two months later under Wood's light fluorescent hairs were observed and M. audouini and M. canis were simultaneously cultured. To our knowledge, this is the first recording of three fungi simultaneously infecting the scalp.

The isolation of T. violaceum appears to be enhanced by the addition of cycloheximide and chloramphenicol to Sabouraud's agar, as was also shown to be the case with other fungi.[13] In 139 duplicate plantings on both Sabouraud's agar and Sabouraud-cycloheximide-chloramphenicol agar from the 88 subjects, T. violaceum was isolated 25 times on an unfortified medium and 31 times on the antibiotic-containing medium.

The microscopic and cultural characteristics of the T. violaceum strains were typical. Infected hairs were either completely packed with large spores ("sack full of nuts") or showed branching chains of fungous hyphae within the hair, the latter probably representing an early stage of hair invasion. Cultures on either Sabouraud's or Sabouraud-antibiotic agar were slow-growing; the center of the colony was at first pale lavender with a gray border, but as the colonies aged the color became darker in various shades of purple. Fully grown cultures were glabrous, convoluted, and raised. Microscopically, the cultures showed only septate, branching filaments with chlamydospores. When a few strains were grown on thiamine-enriched medium,[14] microconidia were formed in small numbers, but the production of fuseaux was not observed.

Comment

The clinical picture seen in our series of scalp infections with T. violaceum did not usually show the classic, "black dot" type of morphology. Infected areas showed various degrees of scaling and erythema with broken-off hairs several millimeters long. Often normal-appearing hairs were also present in these areas. This same clinical picture may also be found with T. tonsurans infection.[15]

The source of the T. violaceum outbreak in this state school for the mentally retarded is unknown, but the organism has been isolated repeatedly since 1953.[12] The large number of infections found here caused by this species of fungus calls attention to the vulnerability of persons in the United States to fungous diseases caused by organisms which often are considered to be mainly of academic interest. The close personal contact necessitated by institutional life may well be a cause of consider-

able dissemination of fungous diseases due to species which otherwise rarely produce disease in the United States.

A surprisingly large number of mixed fungous infections of the scalp was observed during this study. Of 71 subjects with culturally proved tinea capitis, 33 (46%) showed a mixed scalp infection, with four of these each yielding three species of fungi. The prolonged intimate contact among these subjects would appear to facilitate contagion.

Previous authors have reported that x-ray epilation followed by topical medication appears to be the treatment of choice in T. violaceum infections of the scalp.[2] We are following a similar regimen in our series of T. violaceum infections. The results of our therapy will be the subject of a future report.

Summary

The clinical and laboratory findings in an outbreak of tinea capitis in a school for the mentally retarded are described. Trichophyton violaceum was isolated from 44 of 88 subjects with clinical tinea capitis. Thirty-three cases of mixed fungous infection of the scalp were found, including four with a triple mycotic infection.

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Histiocytosis X (Granulomatous Reticuloendotheliosis)

Report of a Case of Chronic Disseminated Reticuloendotheliosis Whose Evolution May Have Some Bearing on the Classification

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Review of Some Problems of Reticuloendothelial Hyperplasia

The reticuloendothelial system of the body responds to numerous stimulating agents by proliferation. This is termed systemic reticuloendotheliosis and occurs specifically in the acute infection of typhoid fever; in the chronic specific granulomas of syphilis, tuberculosis, and leprosy, and in deep mycotic infections of histoplasmosis, coccidiomycosis, etc. When a specific exciting agent is not demonstrable, diagnosis is based on clinicopathological correlations. Such is the case in Hodgkins disease, sarcoidosis, and a group of conditions known individually as Letterer-Siwe disease, Hand-Schüller-Christian disease, and eosinophilic granuloma.

It is now generally accepted that Letterer-Siwe disease, Hand-Schüller-Christian disease (noted hereafter, respectively, as L-S disease and H-S-C disease), and eosinophilic granuloma of bone and other organs represent variations in response to as yet undiscovered etiologic factors. The evolution of this concept has been similar to that which has taken place with respect to forms of sarcoidosis and lupus erythematosus. These clinical syndromes with multiple system involvement have been unified, each under a single nosologic heading. The common denominator for each disease has been the characteristic tissue response, demonstrable histologically.

The integration of eosinophilic granuloma, H-S-C disease, and L-S disease as related manifestations of a single entity by Lichtenstein [22] is a fundamental contribution. His suggestion that these be designated for the purpose of specific reference as histiocytosis X has much merit. The term is brief and inclusive and obviates the need for cumbersome terminology.

The contributions to the histogenesis of histiocytosis X (under its various other names) by Farber,[11] Green,[14] Jaffe and Lichtenstein,[18,22,23] Mallory,[24] and Engelbreth-Holm [10] have been most important in elucidating the common denominator of this basic reticuloendothelial reaction. Specialized case reports, too numerous to detail, and clinical reviews have delineated the variability of form which this tissue response can produce. In the main, the pediatric aspects have been well elaborated,[3,4,12,13,27,33,39] because it is in this age group that most clinical cases occur. The cutaneous,[7,19,20,21,25,31,36,37] skeletal,[10,14,15,18,22] and orificial [8,34] aspects have been presented rather fully because of the fair frequency with which these systems are affected. The gynecologic,[26] specific neural,[28] and pulmonary [2,17,41] phase of histiocytosis X have been the subject of fewer communications, which indicates the rarity of organ damage in these areas in a disease uncommon in

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itself. Radiologic studies have been comprehensive.[6,16,35]

In Lichtenstein's integral concept[22] of histiocytosis X, the allocation of different clinicopathologic variations or combinations, of which our case is one, becomes a reasonable procedure. Instead of singling out the dominant pathologic process (e. g., eosinophilic granuloma, nonlipid histiocytosis, or lipid histiocytosis) or the outstanding clinical pattern, and trying to force an eponym on it, when neither the L-S nor the H-S-C label really fits, one may feasibly employ a dynamic correlation. Thus, eosinophilic granuloma localized in one or several bones seems to be the most benign form of histiocytosis. The process may remain localized, or it may progress to systemic involvement. The disseminated form of histiocytosis X may be acute (L-S type) and terminate rapidly or it may evolve slowly and show features of the H-S-C syndrome. When fully developed, the disseminated chronic form may be equated with the H-S-C syndrome when it is complete; oftener it is not complete. There may be destructive osseous lesions of eosinophilic granuloma or extraskeletal lesions, in the skin for example. There may be acute or subacute episodes simulating an L-S pattern. Or there may be any combination of involvement of bone, skin, mucous membranes (including anal or genital), pituitary gland, brain, lymph nodes, lungs, or liver.

The histologic findings present in the various clinical forms are also variable.[10,15,18,24] The earliest tissue response may be a nonlipid histiocytosis, the picture of L-S disease, and remain so despite the chronic clinical form which eventuates. Or it may be an eosinophilic infiltrate (granuloma) which persists, though the clinical form develops into a disseminated process of subacute or chronic type. Biopsy specimens from multiple sites in a given disseminated case may show in one area eosinophilic granuloma and in another a nonlipid histiocytosis. Whether, when, and how rapidly the histiocytes will undergo lipidization (the fate of the histiocytes in H-S-C syndrome) is unpredictable. So, too, ultimate fibrosis, which ends the pathologic activity, is also not of necessity correlated with torpidity or chronicity of the clinical disease. The clinical syndrome that develops is the direct result of the physical presence in functioning organs of an infiltrate, whether it be eosinophilic, histiocytic, or fibroblastic.

Our attention was drawn to this histiocytic triad by a unique case herein presented. Initially, this case posed a problem in dermatologic diagnosis; as its ramifications unfolded over a period of years, it became a problem in nosology, and this we have attempted to present in accord with certain recent concepts.[11-15,18,22-24,33]

Report of a Case

A 43-year-old white woman was admitted to Bellevue Hospital in November, 1953, with a burning, itching, and crusting eruption of the scalp, of six months' duration, the onset of which she related to a hairdressing procedure. Her symptoms appeared first at the vertex and in four months had spread slowly to involve the entire scalp. In the two months preceding hospitalization an eruption had appeared on the forehead, at the sides of the nose, on the chest, in the axillae, on the lower back, and finally on the vulva and the adjacent skin. She had been under ambulant dermatologic care in this six-month period with an initial diagnosis of impetiginized seborrheic dermatitis and had had what could be considered adequate local and systemic antiseborrheic and antibacterial therapy. She had made no response to treatment and was finally hospitalized.

Fig. 1.—Appearance of scalp on admission.

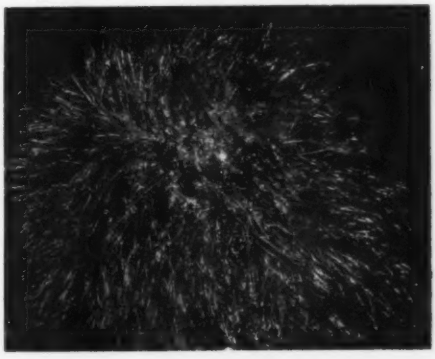

Fig. 2.—Appearance of forehead on admission.

Prior to the scalp trouble she had been well, except for some soreness of the gums and loosening of the teeth which she had noticed a few months earlier.

Examination of the skin on admission showed a thick foul adherent crust over a vegetating base of papules and small nodules covering the entire scalp; a few frank pustules were present at the periphery. There was some slight hair loss. On the forehead, about the nose and mouth, over the chest, on the lower back, and in the axillae was an eruption consisting of fairly dull erythematous papules, 2 to 5 mm. in diameter, each of which had a hard adherent crust that gave a coarse, grater-like feel. Within and about the vulva and in the paranasal and nasolabial folds the papules were grouped, softer, oozing, and vegetating. On the vulva a few pustules were present (Figs. 1, 2, and 3).

There were few other positive findings. A moderate gingivitis was present. The liver was questionably enlarged. A few palpable posterior cervical nodes were found (and related to the scalp infection).

Pending further investigation, three clinical diagnoses were considered: (1) pyoderma complicating seborrheic dermatitis, (2) keratosis follicularis, and (3) pemphigus vegetans.

Treatment was instituted with compresses, several broad-spectrum antibiotics in succession, and 40 to 60 units daily of corticotropin.

Hematologic and chemical laboratory examinations were not contributory. X-rays of the chest and long bones were reported as normal. Biopsy from a paranasal nodule was reported as showing chronic dermatitis, nonspecific.

After the patient had had no response to intense antibiotic and steroid therapy, further biopsy specimens were taken from the scalp, from a papule on the glabrous skin, and from the vulva.

Fig. 3.—Appearance of chest on admission.

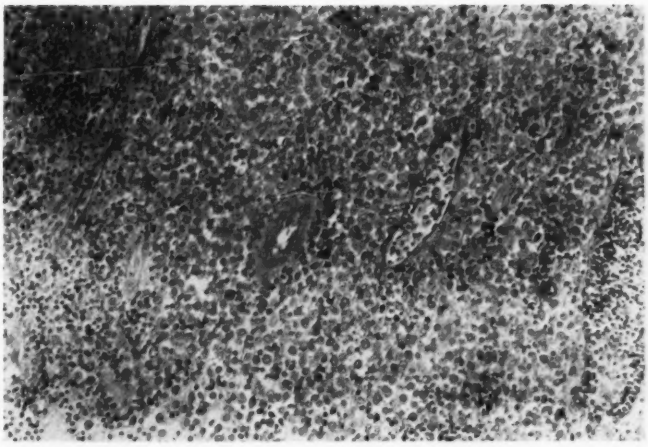

Fig. 4. — Photomicrograph of specimen. Hematoxylin and eosin; reduced about 40% from mag. × 250.

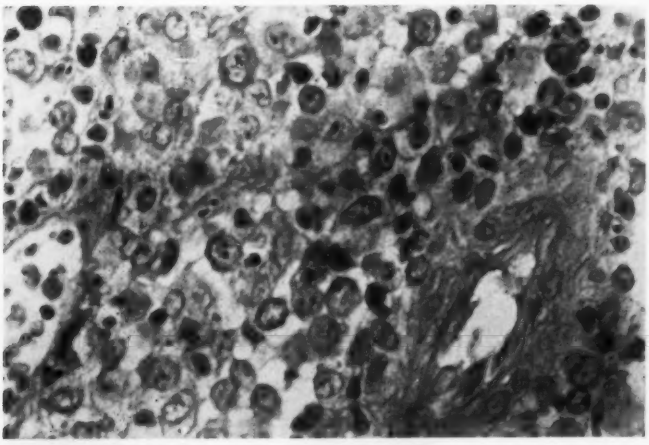

Fig. 5. — Photomicrograph of specimen. Hematoxylin and eosin; reduced about 40% from mag. × 1000.

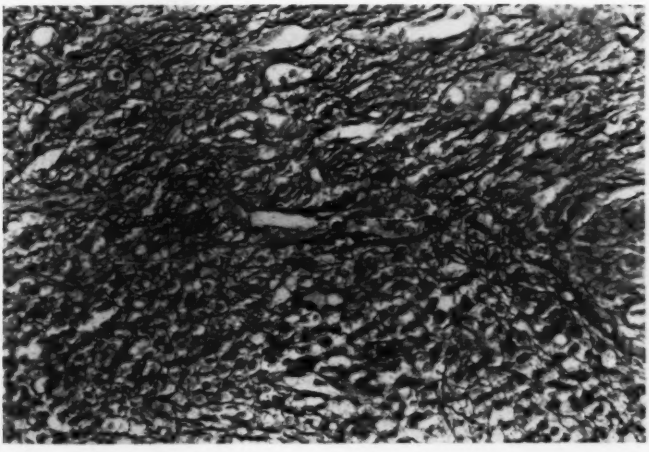

Fig. 6. — Photomicrograph of specimen. Reticulum stain; × 500.

Fig. 7.—X-ray of skull on admission.

Now, in all these, a similar pathologic pattern was seen; throughout the corium was an infiltrate mainly of large histiocytic cells having pale-staining cytoplasm and large vesicular nuclei. There were scattered foci of eosinophilic polymorphonuclear and mononuclear cells with a few lymphocytes and plasma cells. The infiltrate extended to the level of the coil glands. A reactive acanthosis was present in the epidermis. Special staining for reticulum (Foot) showed a finely developed argyrophilic network almost investing each histiocyte. The impression in toto was of reticuloendotheliosis, type undetermined (Figs. 4, 5, and 6).

The histologic findings opened up a fresh diagnostic vista. Now, on specific questioning, the patient said that she had been drinking water and voiding urine a good deal; this was confirmed objectively by a measured fluid intake of 5 liters in 24 hours, followed by an output of 4 liters. The urinary specific gravity was consistently in the range of 1.001 to 1.008. X-ray studies of the skull now disclosed areas of demineralization and irregularly speckled bone rarefaction involving the vault "consistent with Hand-Schüller-Christian Disease" (Figs. 7 and 8).

Exophthalmometry and perimetry were normal. Check on previous laboratory work showed neither glycosuria nor hyperglycemia; total cholesterol was 252 mg. %; cholesterol esters, 156 mg. %. Bone marrow examination was normal.

Since therapy with corticotropin and antibiotics had not been satisfactory, and because of the rather immature histiocytes present, superficial x-ray therapy was administered to the following areas: scalp, vulva, face, and chest. Each area received a total of approximately 300 r given at fractions of 75 r each week between February and April, 1954. Factors used in superficial x-ray therapy throughout were 100 kv., half-value layer 0.8 mm. Al, 25 cm. target-skin distance.

In all treated areas there was excellent resolution of lesions, so that on discharge on April 23, 1954, the patient had only pigmentation on the face and forehead and minimal erythema and thickening of the skin of the anogenital area. The scalp was free of active lesions but showed partial alopecia.

The patient was followed in the outpatient department and had no particular complaint until Aug. 2, 1954, when she noticed discharge and crusting of the ear canals. Otitis externa was found on examination and was related to the underlying reticuloendothelial disturbance. X-ray studies of mastoids and sinuses were made on Sept. 17, 1954, and were reported as negative.

The gingivitis present on her hospital admission, for which she refused treatment, became progressively worse. She also developed erosions on the palate. She was given intense topical therapy at the New York University College of Dentistry. Soreness of her mouth continued to be a plaguing complaint. (The oral manifestations have been reported independently elsewhere.)

The aural discharge was the first sign of a reactivation of disease in her skin. By October, 1954, vegetation and crusting had reappeared on the occipital scalp, forehead, nasolabial folds, chin, ears, retroauricular areas, and left axilla, to a degree warranting further therapy. In view

Fig. 8.—X-ray of skull on admission.

of the previous excellent response to 100 kv. radiation, and anticipating the possible need for repeated courses of radiation therapy, it was decided to use grenz ray, especially since the infiltrate in the skin was very superficial. Face and scalp were treated, each area receiving approximately 2500 r given fractionally at weekly intervals between October and December, 1954. Factors used in grenz ray therapy were half-value layer 0.03 mm. Al, 25 cm. target-skin distance.

By Dec. 10, 1954, all grenz ray-treated areas had involuted nicely. The disease remained under good control until April, 1955. Again the chin showed crusted and vegetative lesions with others in previous areas of predilection on the scalp, face, ears, axillae, and genitalia. The patient was admitted to University Hospital on April 11, 1955. Here systemic reevaluation was not productive of any new information. Again radiolucent areas were found in the skull. Urinary specific gravity remained around 1.010, although active polyuria was not acute. No specific therapy was given, and she was discharged to be followed in the outpatient department.

Because of progressive aggravation of her skin lesions in all involved areas, she was readmitted to University Hospital, on Sept. 8, 1955. System survey showed some suggestion of improvement in the radiolucent skull bone areas; slight linear decalcification was present in the long bones and pelvis. A chest x-ray was negative. Total blood cholesterol was 155 mg. %, with 48% esterified. Therapy was started with prednisone, beginning with 60 mg., gradually decreasing to 25 mg. daily, with some relief, and then with aminopterin, 1 mg. daily for two weeks, without any effect. She was discharged to the outpatient department taking 30 mg. of prednisone daily on Sept. 29, 1955.

On Oct. 17, 1955, she was readmitted for chills and fever commencing seven days prior to admission which had been followed three days later by sudden onset of left facial paralysis and anesthesia. The next day she developed weakness, nausea, vertigo, and hearing loss referred to the left ear. On examination there were numerous papular lesions scattered over the skin of the face and trunk but no vegetating lesions were noted in the previously involved sites. The left ear was draining. The left eye had a large corneal ulcer. There were disturbances of sensation, gaze, and equilibration, all on the left, indicating involvement of the fifth, sixth, seventh, and eighth cranial nerves by some lesion in the cerebellopontine angle.

While she was being studied medically and neurologically, she had a stormy ophthalmologic course; a hypopyon of the left eye developed which fortunately responded to chloramphenicol given by mouth. The corneal ulcer healed slowly; examination on Nov. 29, 1955, showed only a small opacity, which has persisted.

Neurologically, there was first some return of function in the left facial nerve by Oct. 20, 1955. Shortly thereafter there was patchy improvement in sensation over the area innervated by the trigeminal nerve. Cerebrospinal fluid examination was normal in all respects on Nov. 4, 1955. Considering the lack of progression in nerve damage, a neurologic consultant was of the opinion that the cerebellopontine angle lesion was probably not a true neoplasm but part of the underlying reticuloendothelial infiltrate.

Otorhinolaryngologic examination showed the left external auditory canal to be full of debris and lined with dry red skin. Cranial nerve damage as noted above was confirmed.

General laboratory evaluation was again negative for any findings possibly related to the basic disease. X-ray of the skull showed small punched-out areas of diminished density. The lungs were clear radiologically.

Therapy was maintained with prednisone, starting at 75 mg. This was gradually reduced to 40 mg. daily, when corticotropin (ACTH) Gel, 50 units twice daily, was added. At the date of discharge, she was taking prednisone, 30 mg. daily. There had been weight gain of 10 lb., development of some "moon" facies, and dorsal "humping."

On Dec. 2, 1955, she was discharged, feeling generally well but with residual damage in the fifth, sixth, and eighth nerves which has remained. For the next year (1956) she was again an outpatient at the New York Skin and Cancer Clinic. She was treated successively with (1) prednisone, which seemed to give subjective improvement in proportion to the dose; (2) aminopterin, 1 mg. daily for one week in January and February, 1956, without improvement, and (3) grenz ray, 200 to 600 r weekly, to selected areas of active eruption in March and again in October, 1956, with little improvement.

On Nov. 19, 1956, the patient's cutaneous status had become so florid that she was readmitted to the dermatologic service. Again there was scalp, forehead, axillary, and trunk involvement; papules in the exposed sites; vegetations in the moist areas. The vulva was particularly affected. An anal fissure and ulcer were present. Several fingernails were thickened and deformed. The left cornea had residual scarring. Neurologic examination disclosed left-sided partial deafness, facial and corneal hypesthesia with diminished corneal reflex, and anesthesia of the left side of the tongue and palate, all indicating a cerebellopontine angle involvement of left fifth, seventh, eighth, and ninth nerves. Nevertheless, lack of progression led the neurologic consultant again to consider this as a part of Hand-Schüller-Christian syndrome, not a neo-

plasm; surgical intervention was not deemed advisable. Dental examination found a rapidly deteriorating gingivitis, exposing the remaining teeth. Extraction of all the teeth was performed without difficulty or complication. Histologic study of alveolar bone showed fibrous hyperplasia of the marrow and one localized infiltrate of macrophages, plasma cells, and lymphocytes; the macrophages had a foamy cytoplasm which gave a slightly positive stain for lipid with Sudan III. A pathologic diagnosis of reticuloendotheliosis was made.

Laboratory studies were repeated. An occasional white blood cell count up to 15,000, with a normal differential count, was noted. The urinary specific gravity ranged as high as 1.017 (she no longer had any polyuria or polydipsia).

Radiologic study of the skull showed accentuation of the normal stippling, but no radiolucent areas were noted as on previous studies. The chest was negative on roentgen examination.

Biopsy of the skin again showed large clear histiocytic cells in the corium without demonstrable lipid.

The response to local medication with potassium permanganate compresses, antibiotics, and prednisone up to 50 mg. daily was poor. Again superficial unfiltered x-ray therapy was started, on Dec. 10, 1956. Increments of 75 r were given, at approximately weekly intervals, the frequency and total dose being graded to the clinical response. By Feb. 4, 1957, she had received 150 r to the occiput, forehead, and perianal areas; 75 r to the remainder of the scalp, the left axilla, and the right retroauricular area; 225 r to the right axilla and groins; 300 r to vulva; and 450 r to the chin. There was excellent response in all the treated areas. For the first time, pitted scarring was present on the forehead and chin. No scalp hair loss occurred. A few pitted scars were noted on the torso where no x-ray had been given. This scarring was interpreted as the result of spontaneous involution of vascularized papules which had been present.

This patient remained on outpatient care, receiving 10 mg. prednisone daily, until August, 1957, when there was a rapid reactivation of lesions in her usual sites of predilection; she was rehospitalized on Aug. 31, 1957. In addition to a profuse eruption of papules on her scalp, chin, chest, and lumbar region and concentration of lesions about the ears, vulva, and axillae, she had lost weight and was depressed and irritable.

Because of her poor cutaneous state, therapy with superficial unfiltered x-ray was started, while she was once again surveyed systemically. The response was slower and less satisfactory than in previous courses, but by Sept. 20, 1957, definite improvement was noted.

The dose of prednisone was increased to 40 mg. a day at the time of her admission, and, when no improvement appeared, it was reduced and discontinued two weeks later.

Neurologic consultation on Sept. 12, 1957, found disturbance in recent memory and speech, anosmia on the left, bilateral nystagmus, left hypesthesia in the distribution of the fifth nerve, bilateral reduction in hearing, and some generalized motor weakness, suggesting an organic brain syndrome with diffuse involvement of the cerebrum, brain stem, and cerebellum. However, on Sept. 13, 1957, psychiatric evaluation did not find any psychosis or organic brain syndrome present, and as the skin improved the patient's behavior and attitude changed accordingly.

In October, 1957, occasional episodes of exertional dyspnea and weakness appeared. On Oct. 10, 1957, she was transferred to the medical service, where evaluation showed a paralysis of the left diaphragm, giving paradoxic movement, accounting for her dyspnea. X-ray study of the lungs on Oct. 14, 1957, showed, in addition to very limited mobility of both domes of the diaphragm, marked peribronchial infiltration in both lower lung fields, more marked on the right (a lung x-ray on Sept. 17, 1957, had shown no unusual features).

On Oct. 18, 1957, the patient was returned to the dermatologic ward unimproved generally and with her skin in an aggravated state; more lesions had appeared on the scalp and forehead as well as on the chest, where pustulation and crusting were present. Several finger paronychias were present. Superficial unfiltered x-ray therapy was again given. Improvement was slow and unsatisfactory.

On Nov. 4, 1957, an ear, nose, and throat consultant reported a mixed type of deafness, with 38 db. hearing loss, left ear; 36 db. hearing loss, right ear. Eye examination on Nov. 13, 1957, demonstrated no pathology.

The general and cutaneous state remained poor so that on Nov. 28, 1957, in an attempt to gain some ground, prednisone therapy was reinstituted at 60 mg. a day, with rapid subjective and some objective improvement. The dose was gradually reduced to maintenance at the end of two weeks, at 30 mg. a day, and has been continued.

Because of the rather indifferent effect of the last course of conventional x-ray therapy and the continuing activity of the skin lesions, on Dec. 18, 1957, another course of grenz ray therapy was administered.

On Jan. 2, 1958, definite involution of lesions was found in the treated areas, with marked subjective improvement.

Laboratory evaluation, aside from the important radiologic chest findings, was again unimpressive. Although casual urine samples showed a specific

gravity of 1.004 to 1.005, a concentrated specimen went to 1.017. Hematologically, aside from an erythrocyte sedimentation rate of 37 mm. in an hour, no unusual findings appeared. Urinary ketosteroids, 4.7 mg. %, and 17-hydroxyketosteroids, 4.7 mg. %, were reported on Oct. 25, 1957. Serum electrophoretic studies on Nov. 14, 1957, showed α_2-globulin broadened, diffuse, and possibly split, with β-globulin moderately and albumin slightly decreased.

Reexamination of lung by x-ray on Dec. 13, 1957, showed no change in infiltration from that seen on Oct. 14, 1957, but by Dec. 30, 1957, fibrosis and emphysema of both lungs were noted. The heart was normal.

The present outlook for this patient is one of persisting disability necessitating hospitalization, and the prognosis, with the appearance of pulmonary involvment, is guarded.

Comment

The patient presented has had, during approximately four years of observation, involvement of all those organ systems at present known to be affected by histiocytosis X of the Hand-Schüller-Christian form. Nevertheless, she still has not developed the classic triad of the syndrome: She has no exophthalmos; her diabetes insipidus is minimal, and her membranous bone defects are minor.

1. *Mucocutaneous Manifestations.*—These began as an apparent pyoderma of the scalp on a seborrheic base which did not respond to antibiotic medication and then evolved into a bizarre clinical picture suggesting pemphigus vegetans or a severe keratosis follicularis. The essential primary lesion has been a pin-head- to match-head-sized papule, erythematous, with an adherent crust, tending to group in intertriginous areas and, on the scalp, producing oozing vegetations. Recurrences have been frequent and tend to affect mostly seborrheic or intertriginous areas. Persistent vulvar eruption, a frequent site[19,26] of involvement in the adult, with itching and burning, has been present. So, also, the appearance of an anal ulcer points up a bothersome localization.

2. *Dental Manifestations.*—Casual soreness of the gums was, in retrospect, probably the earliest sign in our patient of this disease. It persisted and was followed by oral ulcers and by progressive exposure and loosening of the teeth, which finally necessitated total extraction. Characteristic histiocytic pathology was present in the bone of the jaw and in the oral ulcers. This points up the importance of considering the unusual as well as the commonplace in evaluating persistent oral symptoms.[30,34]

3. *Neurologic Manifestations.*—Sudden onset of vertigo and multiple cranial nerve defects brought up the differential diagnosis of an intracranial cerebellopontine angle neoplasm. The nonprogressive character of the neurologic damage and the partial improvement in sensory functions tended to relate these findings to the underlying histiocytosis rather than to a true neoplasm. Partial anesthesia of the left side of the face, tongue, and palate and some hearing loss persist.

Whereas functional abnormalities due to reticuloendothelial proliferation in the region of the hypophysis and/or tuber cinereum are part of the Hand-Schüller-Christian triad, producing diabetes insipidus frequently and exophthalmos occasionally, as well as bone defect, specific neural involvement is apparently a rarity.[28] The diabetes insipidus in this case has been mild, does not require active medication, and, most promising for general prognosis, has recently disappeared. Urinary specific gravity has risen from a range of 1.005 or 1.008 to 1.017.

4. *Osseous Manifestations.*—Other than the dental complaints specially noted, there have been no symptoms referable to bone. Radiologic findings of translucent areas in the calvarium helped establish the clinical grouping of the case. The disappearance of these clear bone areas after three years appears to indicate healing and so, possibly, a more favorable prognosis. However, bone lesions of the reticuloendothelioses are notably sensitive to radiation, and the calvarial defects were subjacent to a scalp which had received irradiation of

300 to 375 r at 100 kv. Although the depth dose of radiation at the level of bone would be small, it could well have had some lytic effect. Whether the bone lesions healed spontaneously or responded to radiation is, of course, open to speculation.

5. *Pulmonary Involvement.*—In four years of continuing observation, no evidence of pulmonary change was found. Then, during the most recent hospital admission, ushered in by dyspnea, rapidly progressive peribronchial infiltration and fibrosis appeared over a matter of a few weeks (October, 1957, through December, 1957). This completes involvement of such organ systems as are now considered targets of this reticuloendothelial affection. Prognosis becomes poorer with this pulmonary involvement.

6. *Laboratory Findings.*—Histologic examination of the specimens from several sites provided the initial diagnostic wedge. Biopsy specimens from skin, bone, and oral mucosa have, at various times in a four-year course, shown the same basic elements: (1) a primitive large-type histiocyte cellular infiltrate, the cytoplasm clear or slightly foamy, the nucleus distinct and large, with cholesterol not demonstrable and reaction from neutral fat present in one specimen; (2) a greater or less concomitant eosinophilia, in some sections great enough to warrant a diagnosis of eosinophilic granuloma; (3) a scattering of lymphocytes and plasma cells; (4) no notable fibrosis. Thus, essentially a nonlipid histiocytosis and eosinophilic reaction have been dominant.

Aside from the significant histologic findings, the clinical laboratory examinations contributed little to the elucidation of the total picture. Simple urinary specific gravity determinations were compatible with diabetes insipidus, the only item of significance of the numerous chemical, hematologic, and serologic determinations.

7. *Response to Treatment.*—Our experience in this case has covered a wide range of therapeutic agents and modalities. Antibiotic therapy, reportedly effective, especially in acute phases (Letterer-Siwe type),[1,3,4,12,27] has been unsuccessful. Similarly, corticotropin and corticosteroids in considerable dosage for some periods have done little more than give some subjective sense of improvement. Anti-folic acid therapy[27] did little for us. We have not used mechlorethamine (nitrogen mustard).[5] X-ray therapy in the conventional range[6,16,30] has consistently induced clinical involution of skin lesions. Grenz ray therapy, whose use has not previously been reported in reticuloendotheliosis, was most successful initially, less so for interval courses, and again very effective on the last admission after conventional-range irradiation did not produce a desired response.

A large segment of human adaptation lies within the sphere of immunology or antigen-antibody relationship. It manifests itself through three main areas: humoral, mesenchymal, and parenchymal. Under so-called normal circumstances, that is, where there is no discernible aberration of structure or function, we have what might well be called immunity. Humoral changes (immune bodies, chiefly in the globulin fraction of serum protein) may be demonstrable. When, however, there is a disturbance in the equilibrium between humoral, mesenchymal, and parenchymal function, we have clinical syndromes. The so-called collagen diseases and amyloidosis are examples of mesenchymal involvement, precipitation perhaps of the abnormal protein moiety with a chain reaction ensuing from the actual mechanical presence of this "foreign substance" in the ground substance.[38] Diseases like sarcoidosis, multiple myeloma, and the reticuloendothelioses, interfering with parenchymal function, represents a cellular hyperplastic reaction. One person's reaction to antigenic stimulation in one way or other is probably the resultant of his genetic inheritance and his previous environmental exposures.

Summary

A case of histiocytosis X is presented with the following features: (1) unusual

onset with gingivitis, pyoderma, and seborrheic dermatitis of the scalp; (2) diabetes insipidus; (3) membranous defects of the skull; (4) cranial nerve involvement (fifth, seventh, eighth, ninth); (5) dramatic response to superficial x-ray therapy; response to Grenz ray therapy.

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Squamous Cell Pseudoepithelioma (Keratoacanthoma)

A New Clinical Variety, Gigantic, Multiple, and Localized

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Last year (1957) we observed a case which presented an extensive ulcerofungoid lesion of tumoral aspect involving the skin of the sternocostal and pectoral regions. The outer aspect made us think at first of a squamous cell carcinoma and later of blastomycosis. The clinical, anatomical, and mycological tests made to identify these diseases showed that we were dealing with a different condition.

Having weighed carefully the data supplied by the patient, together with the clinical evolution and the microscopic examination, we came to the conclusion that the picture presented by the patient had a great similarity to the disease described by Ferguson-Smith (multiple keratoacanthoma) in the year 1934.

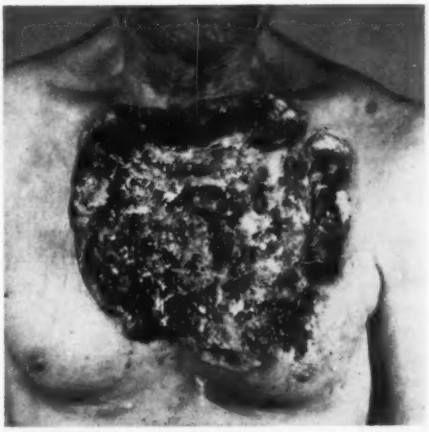

Fig. 1.—Outer aspect of the lesion the first time the patient came to the hospital (May 3, 1958). The height and width of the border are exceptional.

Report of a Case

Clinical History.—The patient, a white Cuban country man, 72 years old, was registered at our hospital on May 3, 1957. He told us that five years earlier he had noticed a raised wart-like nodule, 1 cm. wide, on the skin of the middle sternal region. The tumor, of slow growth, was symptomless. About one year before he came to the hospital, a new group of similar reddish nodules appeared around the first one. These lesions healed toward the central area and spread outward. The involved area, which itched annoyingly, bled a little and had a thick yellowish discharge.

Physical Examination.—The man, of a healthy and muscular appearance, had the sun-pigmented skin frequently seen among our farmers. No keratosis or senile spots were seen.

The lesion consisted of a shallow crater-like ulcer, 7 by 6 in. with a wide (1 in.) and elevated (½ in.) border and flat cicatricial center. It spread from the sternum manubrium and the edge of the clavicle down to the xiphoid appendix and across from one pectoral region to the other. On the left side it extended farther, reaching the anterior axillary line.

The rolled indurated border was covered on the side toward the center with a thick and hard horny excrescence, and on the outside, toward the normal skin, had a reddish, fleshy appearance. An unpleasant yellow discharge was present. When the border was pressed, it exuded drops of pus and plugs of sebaceous-like material as in cases of chromoblastomycosis.

The central part of the lesion, covered by shiny and cicatricial skin, presented multiple and scattered nodules and papule-like lesions. Some were reddish and fleshy, and others, covered with a thick horny coating, resembled keratoacanthoma and the cutaneous horn.

The elastic hardness and the elevation of the border of the lesion had the same appearance and consistency as that of a squamous-cell carcinoma of the skin.

May 5, 1957.—Several biopsies of the border of the tumor were made for histological examination and a culture made on Sabouraud medium for

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Fig. 2.—A close up of the upper third of the lesion, showing details of the border and nodules located in the center of the lesion.

blastomycetes. We also gave the patient penicillin to control the secondary infection and a dose of 1200 r x-rays in order to find out the radiosensitivity of the lesion.

The antibiotic relieved the infection and cleared up the tumor but did not change the general appearance.

Because of the failure of the treatment used, I decided to carry out in a first session the electrosurgical removal of the whole border and later to apply the same treatment to the nodules of the central part. Five days after removing the nodules, there reappeared around the wounded area new nodules with the same characteristics, which received a similar treatment.

July 15, 1957.—Four weeks after the nodules of the central part were removed all this area was epidermized and a series of 20 or 25 new nodules of 1 mm. to 2 cm. diameter had reappeared. This time chlortetracycline (Aureomycin) was given for three weeks without any results, and then intravenous injections of oxophenarsine hydrochloride (Mapharsen) (2.6 mg.) for five weeks, one injection every five days. The latter treatment coincided with reduction and keratinization of a hazelnut-sized nodule that the patient had had and which had remained unchanged for two months. Some months before I had treated with the same drug a solitary keratoacanthoma on the face of a patient and it had disappeared in eight weeks. Those final results in cases belonging to the same disease seem to show that different varieties of it behave in different ways when treated with arsenicals.

I saw the patient again on Sept. 13 and Oct. 12 of the same year, and he had new nodules between 1 and 2 cm. in size. These were treated in a similar manner. The last time that I examined him was on March 15, 1958, and he had a solitary hazelnut-sized nodule of two months' evolution.

Anatomical Examination.—A low-power view of a topographic section of the border of the lesion, perpendicular to the skin surface, shows two different pictures of the inner and outer sides of the border. The former, pertaining to the horny area, is striated and shows a papilla-like process covered with a thick coat of scales and crusts. The outer side, of a flashy and homogeneous aspect, is a cellular hyperplastic zone rich in masses and cords of cells and with fewer scales.

Fig. 3.—Reappearance of multiple new nodules, five weeks after others had been removed (July 15, 1958). The whole area of skin involved had a clearer tinge and cicatricial appearance.

Fig. 4. — Topographic low-power view of two cone-like nodules. The upper shows upward papillary processes and long and narrowed crypts filled with keratin.

Fig. 5. — Topographic low-power view of a round nodule. At the central part of the picture two crypts filled with keratin and opened to the surface of the epidermis are seen. The left one is deeper, irregular and branched. Below it multiple epidermic cell processes spread into the dermis. Prep. No. 24236.

Fig. 6.—A topographic low-power view of the border of the lesion. Acanthosis, papillary processes, and hyperkeratosis are seen. Prep. No. 24235.

Fig. 7.—Another view under higher magnification of a border of the lesion. There may be seen the hyperplastic epidermis and some crypts filled with keratin.

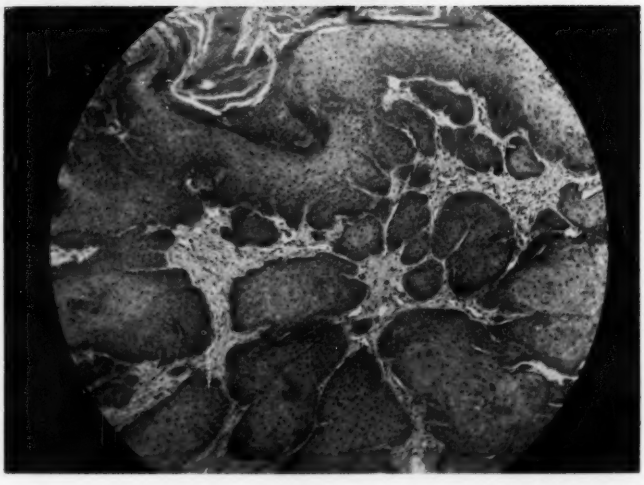

Fig. 8.—A high-power section, perpendicular to the surface of the skin. In the upper part of the picture a depression (crypt) of the hyperplastic epidermis, filled with keratin may be seen. Below many epidermic masses of cells extending into the dermis, like squamous-cell carcinoma are seen. These nest cells, surrounded by a fibrosis stroma having a keratinized central part had a highly differentiated aspect.

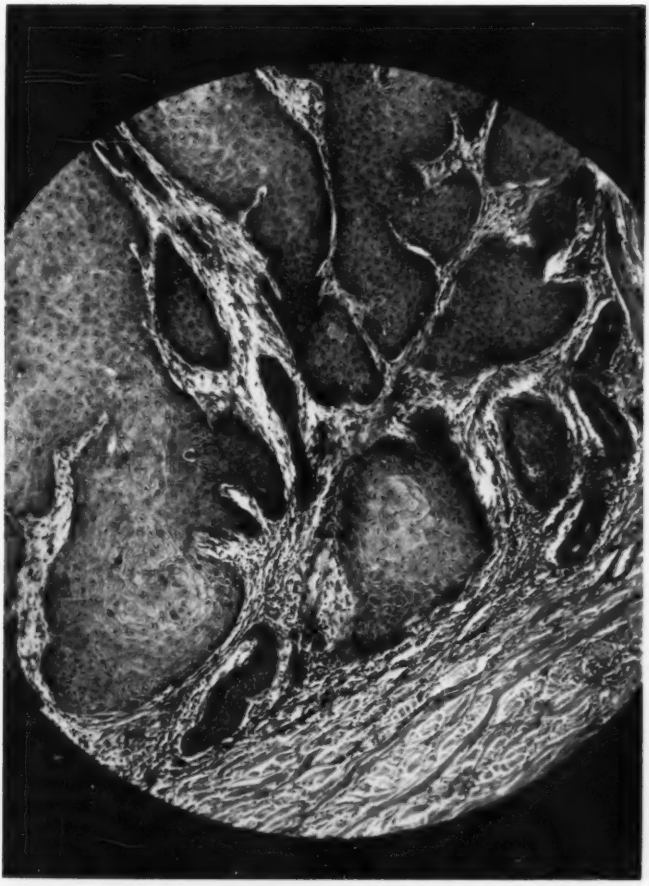

Fig. 9.—A highly magnified view of downward hyperplastic epidermic processes surrounded with round cell infiltration of the neighboring stroma. Also sections of hyperplastic excretory sweat-gland ducts may be seen.

Histology.—The zone of the lesion near the normal border of the skin, under higher magnification, shows the transition between the little-affected epidermis and the hyperkeratotic places. From the hyperplastic epidermis irregular masses and cords of cells proliferate and branch out downward to the dermis, these processes containing much keratin. The horny layer is hyper- and parakeratotic.

Single and irregular branched crypts filled with keratin and surrounded by epidermal cells opened upward to the surface and extended down into the dermis.

The hyperplastic epidermic processes are highly differentiated and few mitoses are seen. A great tendency toward keratin production is observed everywhere.

There is pronounced round-cell infiltration and enlarged blood capillaries in the stroma that surrounds the epidermal cell processes.

A few excretory sweat gland ducts with thick hyperplastic walls can be seen. This change is less frequent and marked than in those keratoacanthomas located on the back of the hands and forearms. The hair follicle changes are negligible.

In some places may be seen epidermal cell processes, in a regressed stage, being replaced by fibrous tissue.

Comments

I am going to comment on the facts, taking into consideration their evolution, and to try to present my interpretation of them according to my personal opinion.

In the first place, the patient stated that the disease started five years before with one or more small wart-like nodules on the surface of the skin of the sternal region. It is to be assumed that in the early stage and for some years the nodules appeared

and grew larger until attaining a certain size. Then they regressed and healed, to reappear later in other places. More recently (about one year before I examined him at the hospital) the nodules began to join together, causing an ulcerated lesion with wide, raised borders that spread from the center to the periphery, healing inward and growing outward. In the central part of the lesion, which presented a cicatricial aspect, new nodules, not more than 2 to 4 cm. in diameter, appeared.

The bulky aspect of the border led me to believe that the cell proliferation on this site needed the presence of a normal skin not previously affected in order to take place.

During the first six weeks that the patient was under my almost daily observation I saw how the central nodules grew and, at the same time, new ones appeared in the neighboring areas, never surpassing a diameter of four cm. Owing to the extent of the area involved, I removed first the raised border and then the central nodules in two sessions. The technique used was a transversal section of the tumor or nodule through the base and electrocoagulation of the wound surface. The latter took about four weeks to heal. Usually, in areas that were healing, new nodules would not appear, although sometimes they would appear near the healing area. Some nodules were seen to grow in five to seven days until they attained 2 or 3 mm. diameter. One month after the last removal of 30 or 40 small nodules located in the central cicatricial area, I treated in the same manner eight new lesions that had appeared.

All the facts mentioned lead to the conclusion that this was a disease with the same clinical characteristics as multiple keratoacanthoma, or Ferguson-Smith's disease. From the evolutive point of view the condition behaved as a spontaneously self-healing tumor. In the present case the lesion healed inward to the center and extended outward.

The masses and cords of hyperplastic cells coming down from the epidermis into the dermis are not infiltrative and do not surpass the level of the hair follicles and sweat gland coils. Besides, lymph-node metastasis do not occur.

The raised border, slowly but uninterruptedly, is healing on the side facing the center and extending on the outside. On the central part of the lesion continually and few days or weeks apart, appear multiple new nodules that grow slowly or fast until attaining a size of 1, 2, or 4 cm., and then some weeks or months later they heal spontaneously.

In this particular case a gigantic ulcerated tumor-like lesion with two different parts was found. The first is represented by a wide and raised border, and the second, in the center and surrounded by the former, by a flat cicatricial area where multiple nodules of different sizes are found. The two parts (border and nodules) have the same microscopic structure, that is, masses and cords of hyperplastic epidermic cells filled with scales. These nodules offer the same histologic picture as that of keratoacanthoma, and in some places remind one of the structure of a well-differentiated squamous-cell carcinoma of the skin.

The outer aspect and fast growth of the nodules are like those seen in Ferguson-Smith's disease.

Some nodules, after reaching a given size, remain unchanged from six to eight months and then regress. Other nodules appear on the border or neighboring area around the surgical wound of the ones removed.

Summary

In this paper a gigantic tumor-like ulceration of wide and raised rolled borders and a flat and cicatricial center covered with scattered multiple fast-growing, self-healing nodules (from 1 mm. to 4 cm. in diameter) is reported.

The clinical and anatomical characteristics gave the impression that this was an atypical localized case of Ferguson-Smith's disease (multiple self-healing squamous-cell pseudoepithelioma of the skin).

The outer aspect of the lesion when I saw it for the first time made me believe that it was a cutaneous squamous-cell carcinoma or a chromoblastomycosis.

The patient was a white man, a healthy-appearing 72-year-old farmer.

The last time I examined him (March, 1958) the lesion had healed with the exception of a horny hazelnut-sized nodule in a state of regression. This regression was, perhaps, a result of the arsenical treatment that he had received in the last six weeks. At that time I got the impression that the lesion was under control because of the several electrosurgical treatments received.

K503, 25-27.

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Location and Re-Formation of the Epithelial Barrier to Water Vapor

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Winsor and Burch [1] studied insensible water loss through the skin after it was removed from the body. They found that light sandpapering, which they claimed removed only the stratum corneum, increased the rate of water loss to approximately the same extent as removal of the entire epidermis. They also found that the roof of an intact cantharides bulla produced as much resistance to water loss as the intact skin. They concluded that the stratum corneum was the main barrier to increased insensible water loss.

Blank,[2] working with abdominal skin in vitro, determined the amount of insensible water loss through normal skin and skin stripped by means of adhesive plaster of part or all of its stratum corneum. Adhesive plaster must remove more of the stratum corneum per unit of stripping than cellophane adhesive tape, since 16 strippings with adhesive plaster were found by Blank to remove the entire stratum corneum, whereas 30 to 35 strippings are usually required with cellophane adhesive tape. Blank found that progressive stripping showed that there was very little change in the rate of water loss until 12 strippings had been removed; 16 strippings produced a much greater increase. Blank concludes that the major barrier against water loss over most areas of the body is a very thin barrier at or near the base of the stratum corneum.

Rothman [3] disagreed with the concept that the stratum corneum is the main barrier to increased insensible water loss. He stated that the transition layers, namely, the stratum lucidum and the stratum granulosum, constitute the main barrier.

The purpose of this work was to resolve this question and to study the re-formation of the barrier after its removal. At the same time, a study was made of the reformation, after stripping, of the superficial barrier to a solution of the anesthetic lidocaine (Xylocaine) base. All of the experiments were done on living human abdominal skin in situ.

Methods and Materials

To determine insensible water loss, a method was employed which was similar to that used by Felsher and Rothman.[4] A glass tube (Fig. 1), 4 cm. in diameter and 10 cm. long, was fitted with a rubber stopper, to the lower surface of which a metal hook was attached. A small bag of cotton material, containing 8 gm. of anhydrous calcium chloride, was placed in a weighing flask, kept in a desiccator, and weighed shortly before use. The

Fig. 1.—Glass tube with small bag containing 8 gm. of anhydrous calcium chloride.

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From the Division of Dermatology, Department of Medicine, University of Miami School of Medicine.

cotton bag had been fitted with a loop by which it could be attached to the metal hook. The glass tube with rubber stopper and attached bag of anhydrous calcium chloride was placed on the skin, and its base was attached to the skin by strips of waterproof adhesive plaster (Fig. 1). At the end of 30 minutes, the bag was removed, placed in its weighing flask, and reweighed. The increase in weight represented the amount of moisture lost by the enclosed area of skin. The room temperature in these experiments varied from 25 C to 28 C but was constant for each experiment. The moisture lost by the skin was expressed as milligrams per square centimeter per hour.

The loss of insensible water was determined on normal skin of the abdomen and also over the same area, stripped over its entire surface of 12.57 sq. cm., with cellophane adhesive tape in increments of 5 strippings to a maximum of 35 strippings.

The loss of moisture was determined over a large granulating varicose ulcer devoid of epithelium. The loss of moisture over a volume of isotonic saline solution was observed by immersing the end of the tube a distance of 1 cm. into the solution. The temperature of the solution was adjusted to 25 C and 35 C.

The re-formation of the barrier to increased insensible water loss was followed by doing determinations 24, 48, and 72 hours after stripping the skin 35 times and in some cases 4, 5, 7, and 14 days thereafter.

Biopsy specimens were taken of normal skin, skin stripped 20 and 35 times, and skin 24, 48, and 72 hours, 1 week, and 2 weeks after stripping.

Re-Formation of Superficial Barrier to Penetration by an Anesthetic Solution.—In a previous article,[6] one of us (S. M.) had shown that, on normal skin, application, in the form of a patch test, of 2% lidocaine base solution in 45% isopropyl alcohol, 10% glycerin, and 45% water produced anesthesia in about 60 minutes. On skin from which the stratum corneum had been removed by stripping with cellophane adhesive tape, anesthesia with the same solution required only a minute or two. Use was made of this fact to determine the rate of re-formation of the stratum corneum barrier to penetration by an anesthetic, as represented by the lidocaine base solution.

At daily intervals for a period of two weeks after complete removal of the stratum corneum, the time required to produce anesthesia in the stripped area with 2% lidocaine base solution was determined. When this time reached 60 minutes, the re-formation of the barrier was considered to be complete.

TABLE 1.—*Insensible Water Loss on Normal and Stripped Skin*

	Insensible Water Loss, Mg/Sq. Cm/Hr.							
		Strippings, No.						
Patient	Normal Skin	5	10	15	20	25	30	35
1	9	7	7	14	27	26	28	28
2	5	4	4	17	21	27	24	27
3	9	9	9	13	19	19	27	28
4	8	12	11	15	20	20	28	28
5	2	2	8	8	21	22	23	29
6	2	2	2	6	13	19	29	28

Results

Table 1 shows determinations of insensible water loss on normal and stripped skin. Figure 2 plots these determinations and shows the average loss. The loss does not increase much in most cases when the skin is stripped 5 or 10 times. With 15 strippings, there is usually a considerable increase, which is greater with 20 strippings and reaches a maximum at 25 to 35 strippings, namely about 29 mg. per square centimeter per hour.

The loss of moisture over a varicose ulcer devoid of all epithelium was 33 mg. per square centimeter per hour.

The loss of moisture over a container of water at 35 C covered with the calcium chloride absorbing tube was 32 mg. per square centimeter per hour.

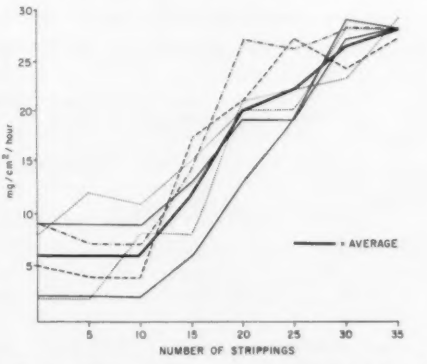

Fig. 2.—Water vapor loss on normal and stripped skin.

TABLE 2.—*Insensible Water Loss After Stripping Skin Thirty-Five Times and at Intervals Thereafter*

Patient	Loss After 35 Strippings	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days
1	28	15	9				5	
2	27	14	5		6			
3	28	17	9				5	
4	28	13	6		5			
5	29	20	10	8				4
6	28	8	6		4			

The marked effect of temperature on this loss is shown by the loss of moisture over a container of water of 25 C, when the amount was only 7 mg. per square centimeter per hour.

Biopsy specimens of skin 24, 48, and 72 hours after complete stripping of the stratum corneum confirmed the findings of Pincus[7] and Lobitz.[8] A few layers of parakeratotic cells formed which were replaced by an anuclear stratum corneum at the end of one week.

Re-Formation of the Barrier to Increased Insensible Water Loss.—The re-formation of this barrier is very rapid. Within 24 hours (Table 2) there is a marked decrease in water loss, from about 29 mg. per square centimeter per hour to about 15 mg. In 48 to 72 hours the loss has diminished to almost normal figures, about 8 mg., with a gradual decrease thereafter. This rapid reformation of the barrier is not associated with normal stratum corneum formation but with the production of a parakeratotic layer of cells. In all probability, the barrier to the loss of moisture is due to the drying-out process of the exposed cell layers and the formation of a thin crust of dried intercellular fluid. At the end of one week the parakeratotic layers have given way to anuclear stratum corneum which then exerts its normal moisture-barrier effect.

Re-Formation of the Barrier to Penetration of an Anesthetic Solution.—The reformation of this barrier is a gradual one, as shown in Table 3 and Figure 3, requiring about two weeks. This is in marked contrast to the rapid re-formation of the barrier to insensible water loss. The drying out of the outer layer of the skin does not prevent penetration by the anesthetic solution, since this drying is immediately counteracted by the water in the solution. The formation of the barrier must await the production of normal stratum corneum, which evidently requires about two weeks.

Figure 3 shows in graphic form the time required for a return to practically normal of the barrier to both insensible water loss and electrolyte penetration. The figures were obtained by plotting the percentage of return to normal against the time in days after 35 strippings.

TABLE 3.—*Time Required to Produce Anesthesia with Two per cent Lidocaine Base Solution on Skin Stripped Thirty-Five Times and at Intervals Thereafter*

	Time Required To Produce Anesthesia with 2% Lidocaine, Min.																
Patient	0 Day*	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	10 Days	11 Days	12 Days	13 Days	14 Days	15 Days	16 Days
1	1			5		8		20			30		40		55	60	
2	2				9	14		31			45		60				
3	2				10	18			30		40		43		45		60
4	2	6			20		30		40			60					
5	2	6			12		20		30		45		60				
6	1			7		15		30		40			50		60		

* Days after stripping.

Comment

It is evident from Figure 2 that the barrier to increased insensible water loss is in the stratum corneum. To place it more exactly, let us figuratively build up the stratum corneum from the stratum mucosum 35 strippings below (Fig. 4). At this point the entire barrier has been removed and the water vapor loss is approximately equivalent to that of isotonic saline solution at the same temperature. This indicates that the epidermis below the stratum corneum is a wet tissue, and it was so recognized by Malpighi as the stratum mucosum malpighi. The amount of insensible water loss from the stratum mucosum in our patients averaged 28 mg. per square centimeter per hour. After the previously stripped 10 layers, from 26 to 35, inclusive (Fig. 4), are added to the stratum mucosum, the insensible water loss has dropped to 22 mg. per square centimeter per hour. These 10 strippings evidently reduce the water loss and therefore constitute part of the barrier to it. When 10 more strippings, namely, from 16 to 25, are added, the amount of moisture passing through falls to an average of 12 mg. per square centimeter per hour. An additional barrier is therefore produced by these strippings. Similarly, the addition of the five strippings from 11 to 15 causes a further decrease of moisture passing through, to 6 mg. per square centimeter per hour.

The 10 strippings constituting the outer third of the stratum corneum do not offer any further barrier to the passage of moisture. We can, therefore, state that the inner two-thirds of the stratum corneum constitute the main barrier to increased water vapor loss from the skin.

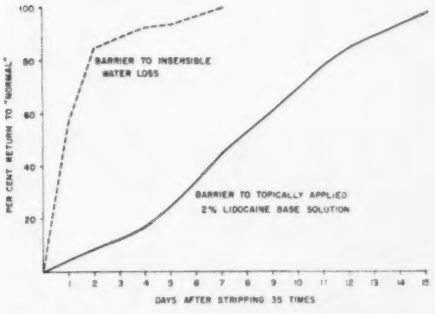
PER CENT RETURN TO "NORMAL"
100
80
60
40
20
BARRIER TO INSENSIBLE WATER LOSS
BARRIER TO TOPICALLY APPLIED 2% LIDOCAINE BASE SOLUTION
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
DAYS AFTER STRIPPING 35 TIMES

Fig. 3.—Time required to re-form skin barriers.

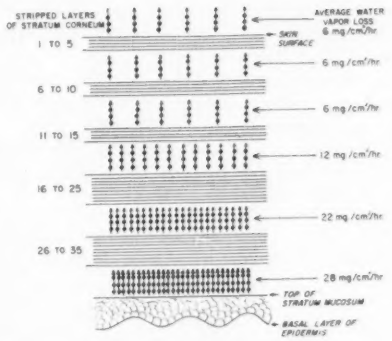

Fig. 4.—Representation of water vapor loss at various depths of stratum corneum.

Summary

The barrier to increased insensible water loss is mainly the inner two-thirds of the stratum corneum.

The epidermis below the level of the stratum corneum is a wet tissue. If the barrier is removed, water will evaporate from it at approximately the same rate as from a free water surface.

The re-formation of the barrier to increased insensible water loss is very rapid, requiring only 48 to 72 hours to return to near normal.

The re-formation of the stratum corneum barrier to superficial epithelial penetration by an anesthetic solution is a gradual one, requiring about two weeks, or until the formation of normal stratum corneum.

University of Miami School of Medicine (36).

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Alopecia Mucinosa

Report of a Case with a Grouped Papular Eruption and Alopecia of the Scalp

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The following case report is felt worthy of presentation as a hitherto undescribed clinical form of alopecia mucinosa consisting of a grouped papular eruption in addition to areas of alopecia. In his original description of this disease, Pinkus [1] reported six cases in which the clinical picture consisted primarily of inflammatory plaques and areas of alopecia. In Lund's case in this group, an accentuation of hair follicles within the area of alopecia was noted. In the case described much earlier by Lehner and Szodoray [2] as "inflammatory follicular edema," keratotic plugs were present in follicles with the inflammatory plaques. Braun-Falco [3] reported two cases of this condition which he has called primary or idiopathic "mucophanerosis intrafollicularis et seboglandularis" presenting inflammatory plaques, and a case of mycosis fungoides and one of eosinophilic reticulosis showing similar pathologic changes.

Grouped small papules as seen in this case have not previously been described. The pathologic changes in both the papular lesions and the areas of alopecia on the scalp were typical of root sheath mucinosis.

Submitted for publication June 4, 1958.

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Report of Case

An 11-year-old white boy of average build was first seen on April 5, 1957, with presenting symptoms of a papular eruption on the back of the neck and a patch of alopecia on the left temporal area of the scalp. The eruption on the back of the neck had been present about three or four months, while the spot of alopecia was noted about one month previously. Both lesions were asymptomatic. On cursory examination, the eruption on the back of the neck could easily have been mistaken for a plaque of lichen simplex chronicus. However, on closer examination and particularly with the head bent down, the entire area was seen to consist of closely set, small, slightly elevated, dome-shaped, flesh-colored papules about 1 or 2 mm. in diameter (Fig. 1). They were, for the most part, arranged

Fig. 1. — Back of the neck. Note "bristle hairs" near the scalp line.

Fig. 2.—Small area of alopecia in the temporal region.

in short horizontal or slightly curved lines. There was no visible inflammation. The patch gradually merged with the surrounding normal skin. One interesting feature was the presence of short "bristle" hairs in the area particularly near the scalp line. The spot of alopecia was an ill-defined, slightly scaly area about 2 cm. in diameter, within which were some broken-off and other full-length hairs, many of which could be easily and painlessly epilated (Fig. 2). Tinea capitis was suspected, but Wood's light examination showed no fluorescence. Direct examination of the scales and hairs with 10% potassium hydroxide solution failed to show hyphae or spores, and repeated cultures on Sabouraud's agar produced no fungus or other growth. However, microscopic examination of the hair roots showed a peculiar dystrophy, which will be described in more detail under "Pathology."

The eruption on the posterior neck failed to improve after three weeks with a 2% pine tar and 2% salicylic acid ointment, and a 3 mm. punch biopsy specimen was taken from this region. The typical pathologic changes of alopecia mucinosa as previously described by Pinkus[1] were found. On the patient's visit on May 7, a new area of scaly alopecia about 3 cm. in diameter on the posterior right parietal region was noted (Fig. 3). Again many hairs within and at the borders of the alopecia could be easily and painlessly epilated, and microscopic examination showed the same peculiar dystrophic changes of the hair roots. Again there was no evidence of fungus infection by di-

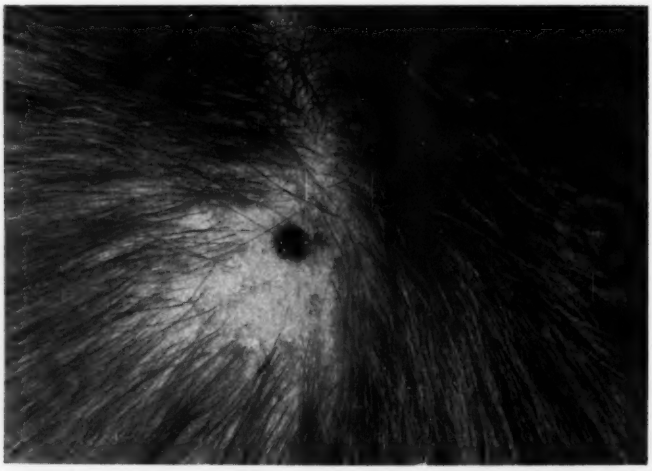

Fig. 3. — Alopecia of parietal area. Some fine scales can be seen. Crust represents biopsy site.

Fig. 4.—Popliteal area.

Fig. 5.—Inner right knee.

rect examination or planting of hairs on Sabouraud's agar. Wood's light examination was negative.

During the month of May, the patient was carefully examined for other evidences of this disease, and other groups of small flesh-colored papules no larger than 1 or 2 mm. in diameter and all asymptomatic were noted in both popliteal spaces (Fig. 4), the medial right knee (Fig. 5), and inner left-upper buttocks. Less well defined areas of follicular papules over the sacral and lumbar regions were present. Both elbows were dry and rough.

In view of previous success with superficial roentgen therapy in some cases of alopecia mucinosa,[1] the area on the inner aspect of the right knee was given a course of four weekly treatments of 75 r at 90 kv. There was a 50% involution by the fourth week, and the patch had completely disappeared several months later. Six similar treatments at weekly intervals were also given to the left popliteal area, but while about a 50% improvement was obtained, the papules could still be seen six months later.

By June, 1957, the temporal area of alopecia had completely regrown, and by July, 1957, the parietal area had regrown. Thus both areas showed complete spontaneous regrowth within two to three months after they were first noted.

In December, 1957, a new group of discrete small flesh-colored papules about 1 mm. in diameter covering the ventral surface of the shaft of the penis was noted. These were asymptomatic and unknown to the patient.

By May, 1958, 17 months after the eruption was first noted, and 14 months after the patient was first seen, the papular involvement on the back of the neck and both popliteal areas was still visible though less distinct than when first seen. The newest group on the penis was still well defined. The patches on the right knee, buttocks, sacral and lumbar areas had cleared. No new areas of alopecia had developed. A course of thyroid, grain ¼ (15 mg.) daily for five weeks in April and May, 1958, had no effect on the eruption.

Pathology

The characteristic pathology of alopecia mucinosa as reported by Pinkus was found in biopsies of papules from the back of the neck, popliteal area, and area of alopecia of the scalp. The main pathological features from all three areas were edema and mucinous degeneration of the hair follicles and sebaceous glands with the formation of frank mucinous cysts within these structures. A moderate-inflammatory infiltrate was present. The epidermis was relatively unaffected.

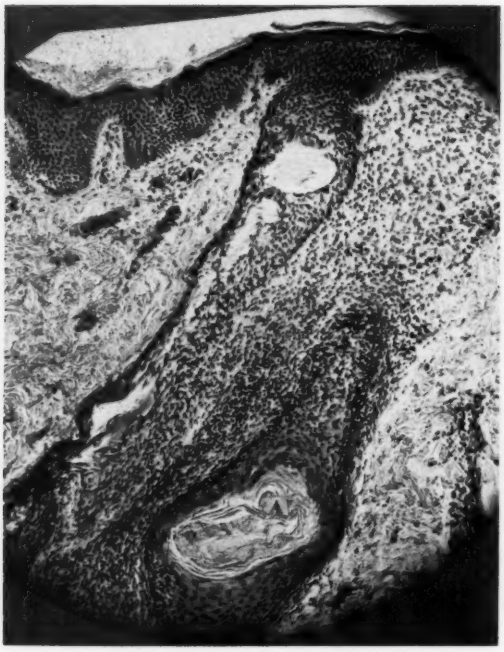

Fig. 6.—Biopsy from back of the neck showing string of mucinous cysts within hair follicle and large mucinous cyst at *A*; hematoxylin and eosin; mag. × 90.

Biopsy from papules on the back of the neck (Fig. 6) shows extensive edema of the hair follicle, with the formation of a chain of small and large cysts throughout the length of the follicle containing stringy pale basophilic material (hematoxylin and eosin stain) which suggested mucin. The sebaceous gland at (*A*) has been transformed into a mucin-containing cyst. There is moderate-inflammatory infiltrate in the surrounding tissue, and only mild perivascular infiltrate in the corium.

Biopsy from the area of scalp alopecia showed mucinous edema and cyst formation in the outer root sheaths of many hairs. No sebaceous glands could be seen. Some follicles contained keratotic plugs below the skin surface. There was mild perifollicular inflammation. Figure 7 is a close-up of a mucinous cyst of a hair follicle.

Biopsy of a popliteal papule showed changes similar to those from the neck and scalp. Figure 8 shows a hair follicle exhibiting marked edema of the root sheath, especially of the middle part including the sebaceous gland. The gland contains none of the usual foamy cells, but contains a cystic space (*C*) partly filled with coagulated basophilic material, and otherwise consists of stellate cells separated by edema. There is considerable lymphocytic infiltration around the follicle. The combination of Alcian blue, which is believed to be a selective stain for acid mucopolysaccharide,[4] and periodic acid-Schiff (PAS) stain showed bright blue material in the cyst and also between the edematous cells of the root sheath. This, of course, cannot be appreciated in the black and white photomicrographs. The PAS stain alone revealed considerable positive granular material in the root sheath. This could be dissolved by pretreatment with diastase and is thus identified as glycogen. Figure 9 is a close-up of the root sheath just above the mucinous cyst showing marked edema and separation of stellate cells.

Fig. 7.—Biopsy from parietal alopecia showing close-up of mucinous follicular cyst; hematoxylin and eosin; mag. × 180.

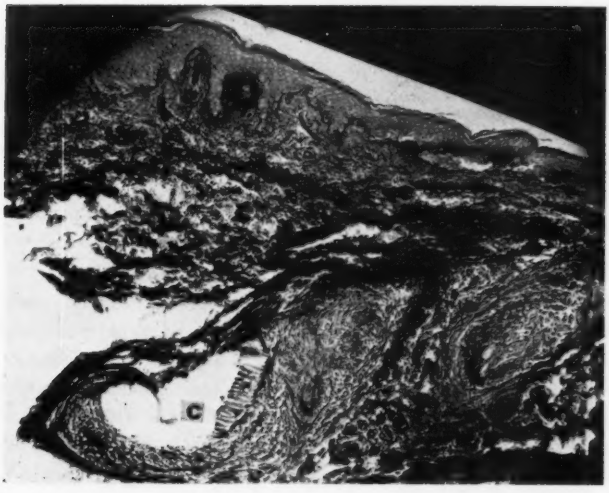

Fig. 8.—Biopsy of popliteal papule. Cyst *C* contains Alcian blue positive material on the right. Adjacent to cyst is edematous root sheath. Alcian blue—periodic acid-Schiff stain; mag. × 90.

Fig. 9. — Close up of edematous root sheath from popliteal papule. Alcian blue-periodic acid-Schiff stain; mag. × 270.

Hair Root Changes

Of particular interest also were the peculiar dystrophic changes seen in the roots of hairs removed from within and at the borders of the area of alopecia of the scalp (Fig. 10). These changes are undoubtedly due to the interference with normal growth of the hair by the pathological processes within the follicle. These hairs were removed easily and painlessly in considerable numbers.

The short "bristle hairs" seen on the back of the neck showed a thick keratinous sheath around the hair shaft above the skin surface, but no dystrophic changes in the hair roots.

Laboratory Examinations

Blood count: hemoglobin 15.0 gm.; white blood cells 6700 (filamented polymorphonuclear leukocytes, 55%; nonfilamented, 4%; lymphocytes, 37%; eosinophils, 4%). Urinalysis: specific gravity 1.021, pH 6.5, rare WBC, a few epithelial cells, albumin and sugar negative. Blood chemistry values were all within normal limits: cholesterol 186 mg. %, total lipids 702 mg. %, dextrose 80 mg. %, total serum proteins 9.0 gm. (albumin 6.0 gm., globulin 3.0 gm.), total bilirubin 0.4 mg., bilirubin one minute 0.1 mg. A starch gel serum electrophoretic pattern showed a slight elevation of the beta fractions, but was otherwise normal. Gamma globulin, determined immunochemically,[5] was slightly elevated, at 15.3 mg. per ml. (normal 10-14). Orosomucoid, the principal mucoprotein of serum,[6] value was 60 mg. per 100 ml. of serum (normal 50-120).

Two 24-hour urine specimens were analyzed for excretion of acid mucopolysaccharide. After dialysis and precipitation with protamine, the uronic acid content of the mucopolysaccharide was 7.45 and 7.54 mg., with use of the orcinol method of de-

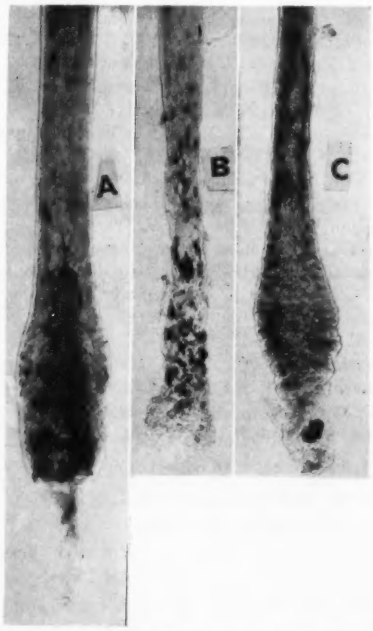

Fig. 10.—Hairs from area of scalp alopecia. *A* and *C* are apparently distorted club hairs, and *B* is a malformed growing hair. The black areas are air spaces.

termination, corrected for hexose. This is in the normal range for boys of this age group as found by Di Ferrante and Rich.[7]

Suspensions of biopsy material from popliteal papules from this patient and from an infiltrated plaque on the neck of another case of alopecia mucinosa recently observed were inoculated into monkey kidney tissue cultures, incubated for seven days in Eagle's medium with 10% bovine serum and observed for seven days. No cellular changes or cytopathogenic effects indicative of virus growth were observed.

Comment

That the pathological picture of root sheath mucinosis may be found in a grouped papular eruption adds another entity to the list of differential diagnoses of papular and follicular eruptions. The papules in this case, particularly in the popliteal areas, back of the neck and ventral surface of the penis being very small and flesh-colored were quite suggestive of lichen nitidus. However, the surface of the papule was dome-shaped and not flat and shiny as is usually seen in lichen nitidus. The less-well-defined patches of follicular papules on the knee, buttocks, and lower back, together with a roughness of the elbows was somewhat suggestive of keratosis pilaris, though the distribution was not that usually seen in the latter condition.

Alopecia mucinosa must also be considered in any scaly alopecia of the scalp. Examination for fungi is negative. The hairs in the affected follicles come out easily, and the peculiar dystrophic changes in the hair roots which can be seen on direct examination may be a valuable clue in the diagnosis. Spontaneous regrowth of hair occurred in from two to three months from both areas of alopecia. It also occurred in one case of Pinkus' group.

There was spontaneous disappearance of papular lesions from some areas, but papules on the neck and popliteal regions were present 18 and 12 months, respectively, after appearance. Response to x-ray therapy in this case was not consistent. One papular group disappeared after four fractional treatments, but another persisted after six similar treatments.

Search for etiologic factors was negative. Blood count, urinalysis, and various blood chemistries were for the most part normal. Urinary excretion of acid mucopolysaccharide and the orosomucoid content of the serum were within normal limits. Studies for virus infection were negative by the methods employed. The cause of alopecia mucinosa has yet to be determined, though it is apparently a benign condition.

Summary

A case of alopecia mucinosa presenting both a grouped papular eruption and two areas of alopecia on the scalp is presented. The pathological changes of root sheath mucinosis, typical of this condition, were found in biopsies from both types of lesions.

No evidence of metabolic disorder or virus infection was found by the techniques employed.

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Hermann Pinkus, M.D., gave the pathological interpretations; Fred L. Rights, Professor of Microbiology, Wayne State University, performed the virus studies; Alfred J. Bollett, M.D., Assistant Professor of Medicine, Wayne State University, did the determination of the urine acid mucopolysaccharide, and Morris Goodman, Ph.D., performed the determination of the serum orosomucoid and gamma globulin.

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Capillary Alterations in Pigmented Purpuric Disease of the Skin

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Of the numerous diseases with purpuric manifestations, pigmented purpuric disease of the skin is of particular interest to the dermatologist, since there are usually no associated hematologic defects and arterial or venous insufficiency does not appear to be related to the eruption. There are three described entities which can be grouped together as pigmented purpuric disease because of their many similarities.[1] This group includes purpura annularis telangiectodes (Majocchi), peculiar progressive pigmentary disease (Schamberg), and pigmented purpuric lichenoid dermatitis (Gougerot and Blum). All three have in common the appearance of minute red puncta in the skin as the primary lesion. In addition, they are characterized by their usual location on the lower extremities and the occurrence of purpura and hemosiderin deposition in the skin. The criteria by which pigmented purpuric disease is subdivided consist of differences in the clinical appearance that can be regarded as variations in degree of the same pathologic process. This concept is supported by the similarities in histopathologic changes found in the three conditions. Angioma serpiginosum is also characterized by the presence of minute red puncta in the skin, but there is no associated purpuric phase, and, for this reason, it is separate from pigmented purpuric disease.

We have studied 12 patients with the clinical manifestations of pigmented purpuric disease, using a modified technique of capillary microscopy.[2] This technique permits in vivo examination of the superficial vascular bed in normal skin and in skin involved by disease. The vascular changes in pigmented purpuric disease adhere to characteristic patterns. The alterations found correlate well with the clinical stage of the disease process in the area examined. No basis has been found for subdividing pigmented purpuric disease into different categories.

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Subjects and Methods

A total of 12 patients with skin findings characteristic of pigmented purpuric disease were studied by capillary microscopy. Lesions on the legs and arms of these patients in various phases of evolution from the minute erythematous puncta to the final atrophic and ectatic stage were selected for examination. The skin was prepared for in vivo microscopy by first removing the keratin by repeated applications of cellulose tape. This procedure has been found greatly to improve the visibility of the capillaries and the subpapillary plexuses of the vessels, and the technique exposes several hundred vessels for examination in each area. The vessels usually are not altered by the application of the tape. Capillary microscopy of the nailfold vessels was also performed on each patient. The superficial vascular bed in normal areas of skin on the lower extremities of the patients was examined by this technique. A tourniquet test was performed on each patient. Blood studies on the patients included a complete blood cell count, platelet count, and bleeding and clotting times.

Observations

Clinical.—The Table presents the pertinent clinical data on the patients who were studied. We classified our cases as pigmented purpuric disease if there were red puncta present, a petechial or purpuric phase occurred in the absence of demonstrable hematologic defects, and there was subse-

Summary of Findings in Twelve Patients with Pigmented Purpuric Disease

Case No.	Sex	Age	Types of Lesions	Distribution	Duration	Hemogram	Tourniquet Test	Symptoms
1	M	30	Puncta, petechiae, hyperpigmentation, atrophy, ectasias	Legs, thighs, trunk, arms	5 yr.	Normal	Positive	None
2	F	38	Puncta, petechiae, hyperpigmentation, atrophy, ectasias, lichenification	Feet, legs, thighs	5 yr.	Normal	Negative	Pruritus
3	M	22	Puncta, petechiae, hyperpigmentation	Feet	6 mo.	Normal	Negative	None
4	M	45	Puncta, petechiae, hyperpigmentation	Legs, thighs	6 mo.	Normal	Negative	None
5	F	14	Puncta, petechiae, hyperpigmentation, atrophy, ectasias	Legs, thighs, forearms	2 yr.	Normal	Negative	None
6	F	45	Puncta, petechiae, hyperpigmentation	Legs, thighs	1 yr.	Normal	Negative	None
7	M	42	Puncta, petechiae, hyperpigmentation	Feet, legs	2 mo.	Normal	Negative	None
8	M	34	Puncta, petechiae, hyperpigmentation	Legs, feet, arms	6 mo.	Normal	Negative	Pruritus
9	M	34	Puncta, petechiae, hyperpigmentation, atrophy, ectasias	Legs, trunk, arms	18 mo.	Normal	Positive	None
10	M	25	Puncta, petechiae, hyperpigmentation	Legs	1 yr.	Hb. 20.6 Hcrt. 64 RBC 7,000,000	Negative	None
11	M	70	Puncta, petechiae, hyperpigmentation	Legs, feet	9 mo.	Normal	Negative	None
12	M	67	Puncta, petechiae, hyperpigmentation	Legs, feet	35 yr.	Normal	Negative	Pruritus

quent hemosiderin pigment deposition in areas of skin previously the site of purpura. Since all of the patients had a purpuric phase, none could be further subclassified as angioma serpiginosum. In several of the patients, there was a tendency for some of the lesions to be annular, and atrophy together with ectasias was not uncommonly seen. These patients classically would be considered to have Majocchi's disease, while another with lichenification present in some involved sites might be grouped as pigmented purpuric lichenoid dermatitis of Gougerot and Blum. Patient 10 was the only subject who had abnormal findings on examination of the blood. The red blood cell count, hemoglobin, and hematocrit were increased above normal (Table). There was no defect of the clotting mechanism demonstrable. The association of pigmented purpuric disease with polycythemia has previously been noted.[3,4]

A tourniquet test was performed on each subject by applying a pressure cuff to an

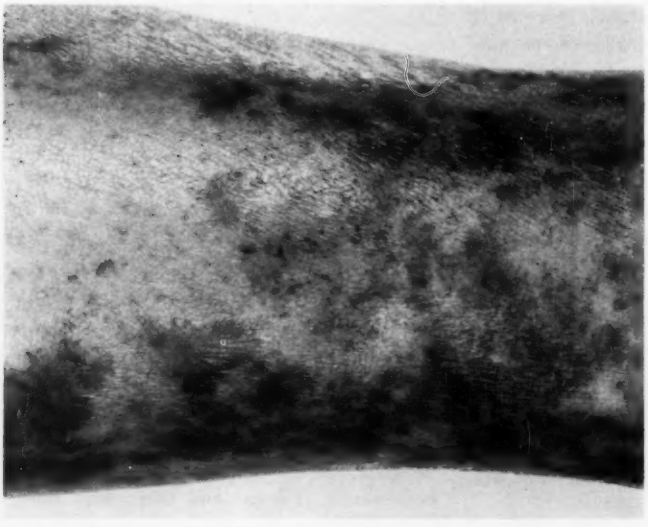

Fig. 1.—Clinical findings in pigmented purpuric disease. Characteristically, there are red puncta, petechiae, hyperpigmentation, minimal atrophy of skin in areas, and ectasias. The lower extremities are the commonest site, and there is an absence of venous and arterial disease.

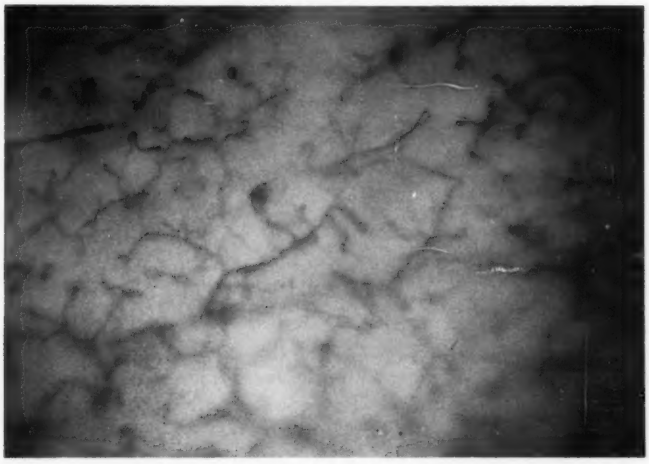

Fig. 2.—The appearance of the capillary bed in an area of normal skin on the leg of a patient with pigmented purpuric disease. Even in this grossly normal area a few capillaries have circumscribed areas of dilatation and there is a petechia forming about one of these ballooned capillaries. Reduced 15% from mag. × 35.

extremity and maintaining a pressure midway between the sytolic and diastolic pressures for three minutes. Two of the twelve subjects had positive findings with this test.

The clinical manifestations seen in a patient with pigmented purpuric disease (Fig. 1) can be correlated with alterations in the superficial vascular bed of the skin when studied by capillary microscopy. The initial vascular change consists of aneurysmal dilatation of the dome portion of a number of end-capillaries visible clinically as red puncta. Rupture of these abnormal capillaries is associated with the purpuric phase of the disease. Hemosiderosis localized to the areas of involved skin constitutes the next recognizable phase. Progressive destruction of the end-capillaries and dilatation of the subpapillary vessels are the vascular changes in the final stages witnessed clinically as atrophic and ectatic skin.

Vessels in Normal Skin.—The vascular bed in areas of skin with varying types and degrees of involvement were studied by capillary microscopy. The nailfold capillaries and normal skin adjacent to lesions were examined.

The nailfold capillaries in all the patients appeared anatomically normal. The end-capillary loops and the vessels of the sub-

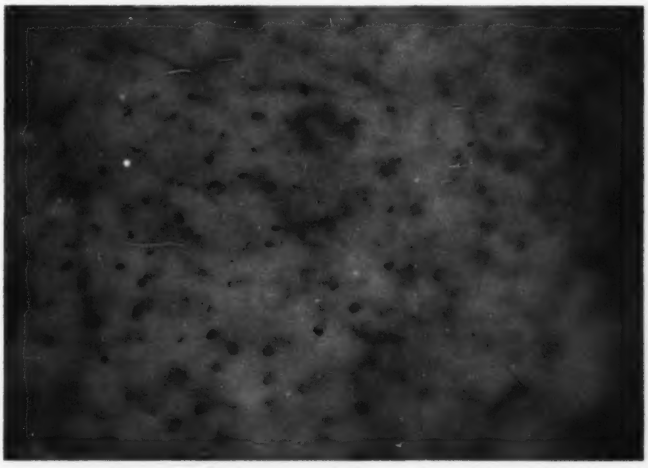

Fig. 3.—The findings on capillary microscopic examination of areas of skin where the predominant clinical finding is numerous minute red puncta. The puncta can be seen to represent aneurysmal dilatation of the dome portion of the papillary capillaries. Reduced 15% from mag. × 35.

papillary plexuses in uninvolved areas of skin either distant from or adjacent to lesions were usually normal. A few capillaries in these normal areas exhibited minimal deformity. This deformity consisted of a circumscribed dilation of a portion of the end-capillary, which was usually limited to the loop portion of the vessel (Fig. 2).

Phase of Aneurysmal Capillary Dilatation.—Examination of the vascular bed in an area of skin where the predominant clinical finding consisted of small red puncta from pinpoint to pinhead size revealed altered capillaries. The changes consisted of bulbous dilatation of the dome portion of many individual capillaries (Fig. 3). Each red puncta seen grossly was a dilated capillary dome microscopically.

A bulbous deformity occasionally was seen to involve the venous capillary limb rather than the dome portion of the vessel. These aneurysmal dilatations of the capillaries were persistent during the period of observation. Engorgement of the superficial vascular bed produced by a tourniquet was not required for the dilatation to be apparent. The size of the dilated portion could be increased, however, by stasis, and this increase was transitory. The number of end-capillaries which appeared abnormal in any one field varied with the stage of the disease.

Where the disease process in the examined site was in an early stage, the subpapillary vessels appeared normal. At no stage did we see bulbous deformity involving the vessels deeper than the superficial capillaries. Some of our patients had lesions including red puncta on the upper extremities. The capillary changes in these lesions were the same as those occurring in lesions on the lower extremities.

Purpuric Phase.—Application of a pressure cuff to an extremity having red puncta, the cuff being left in place for three minutes, did not cause rupture of the deformed capillaries, except in the two patients recorded as having positive tourniquet tests. In five of the patients with negative tourniquet tests, negative pressure applied to skin of involved sites for 30 to 45 seconds did cause rupture of the capillaries at the site of aneurysmal dilatations (Fig. 4). The leakage of the formed elements of the blood out of the capillaries then appeared as petechial hemorrhages.

Hyperpigmented Phase.—Figure 5 represents the vascular bed in a lesion which clinically was a hyperpigmented area. The pigment appears as numerous fine granules irregularly distributed through the tissue. There is a marked decrease in the number of end-capillaries present in this site. Those that remain are somewhat dilated and de-

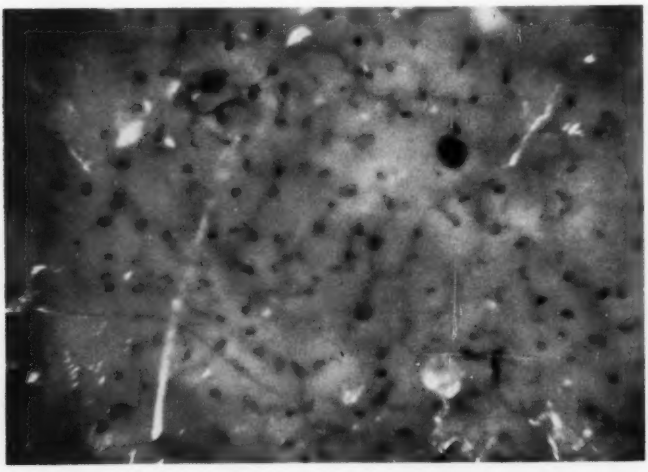

Fig. 4.—A capillary bed with dilated capillary domes, showing effects of negative pressure on the vessels. Several of the capillaries are more markedly dilated and some vessels have begun to leak blood into the tissue to form petechiae. Bleeding occurs at the dilated capillary dome. Reduced 15% from mag. × 35.

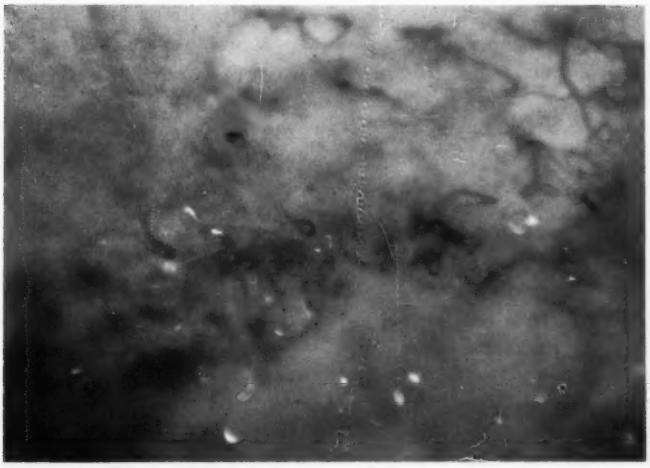

Fig. 5.—The capillary bed in an area of skin in which the clinical appearance was characterized by hyperpigmentation and minimal atrophy. The numerous small granules are the hemosiderin deposits. Note the marked decrease in the number of end-capillaries present and dilatation of the venous portion of those capillaries which are seen. In right upper quadrant the subpapillary plexus is visible with few papillary capillaries arising from it. Reduced 15% from mag. × 35.

formed. There is no evidence that capillary regeneration has taken place in this site. Some subpapillary vessels are visible, and they are almost devoid of end-capillaries.

Atrophic Phase.—Figure 6 represents the vascular bed in a lesion which has progressed to atrophy of the skin, and minute telangiectasias are grossly visible. Almost no end-capillaries remain. The subpapillary vessels appear more prominent than in normal skin. These dilated subpapillary vessels are clinically seen as telangiectasias. They are not newly formed vessels. In none of the areas studied did we see the formation of new capillary vessels to replace those which were destroyed by the disease process.

Intravascular Clumping.—In all patients, intravascular sludging was observed, not only limited to the vessels within lesions, but also in the capillaries of the normal skin and in the nailfold capillaries. Alterations in the degree of sludging did not correlate with the state of the eruption. It was observed during periods when many new petechiae were developing and was also witnessed in some patients who were not developing new petechiae at the time of examination. A granular flow or intravas-

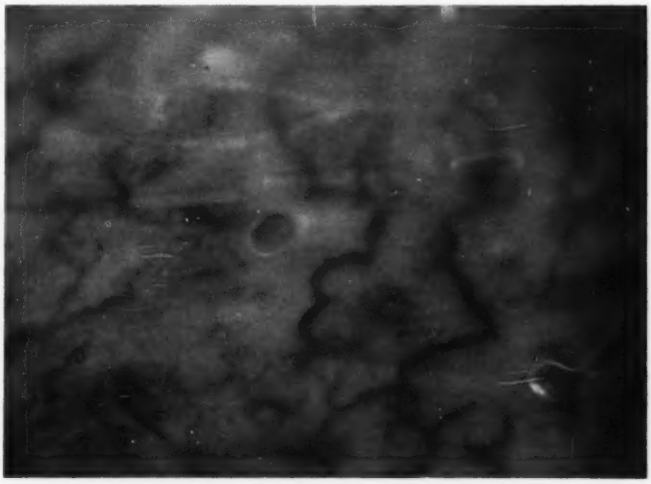

Fig. 6.—The final stage in the evolution of skin changes characteristic of pigmented purpuric disease. In this lesion the epidermis and upper corium are atrophic, and this is most probably secondary to the destruction of the end-capillaries. The ectasias which are grossly visible in these areas can be seen to be the subpapillary plexus, the vessels of which are somewhat dilated. There is considerable hemosiderin deposition which appears granular. Reduced 15% from mag. × 35.

cular clumping of the formed elements of the blood can be induced or, if present, markedly increased by the application of a tourniquet to produce venous stasis in the extremity. No stasis was produced in this manner during our observations. The degree of sludging can vary from only an occasional clump of cells passing into an end-capillary to the continuous presence of a granular stream in capillaries. The rate of flow of the blood through the end-capillaries appeared to be decreased. At times a large clump of cells was seen to enter a capillary and lodge usually in the dome portion, where it would halt the flow of at least the formed elements of blood through that channel for periods of time up to a minute. The phenomenon of sludging was observed to be somewhat more pronounced in those vessels located in the sites of lesions. At this point it is well to recall that in observation of the superficial vascular bed of the skin by microscopy the vessel walls are not visible and one sees only the blood filling the vessel. Because of this, any effect which the passage of a granular stream through a capillary may have on the vessel wall is not directly seen. Those effects on the characteristics of the stream and rate of flow are witnessed.

Comment

The progression of changes in the superficial vascular bed of the skin can be correlated with the clinical appearance of the lesions in patients with pigmented purpuric disease. The primary pathological alteration we have observed in early lesions is an aneurysmal dilatation of the dome portions of end-capillary loops. This dilated portion of the end-capillary is situated in the vault of a dermal papilla and clinically appears as a minute red punctum from pinpoint to pinhead in size.

Rupture of these dilated and weakened capillaries results in small hemorrhages into the upper corium which then appear grossly as petechiae. This is the second stage in the series of changes. Blood pigments are deposited in the corium as an aftermath of the hemorrhages, and incomplete removal results in widely varying degrees of more or less persistent hemosiderosis in the skin. Rather than rupture of the end-capillaries, thrombosis of the capillary also can occur. In either case, we have not witnessed the formation of new end-capillaries to replace those which have been destroyed. Late-stage lesions are found to be devoid of end-capillaries, or only a few remain. Frequently there is a compensatory increase in the diameter of the venules at the level of the subpapillary plexus. Depending on the degree of atrophy of the upper corium, the amount of pigment present, and the thickness of the overlying epidermis and keratin, these dilated venules may appear as ectatic vessels clinically.

It is evident from studying the clinical course of patients with pigmented purpuric disease that there is a wide variation in the degree of progression of individual lesions and there is also a difference found from patient to patient. Individual lesions in patients with the Majocchi variety of pigmented purpuric disease demonstrate a greater propensity to eventuate in atrophy and ectasias. In our experience it is not uncommon to find at least a few atrophic areas with visible ectasias in Schamberg's type of pigmented purpuric disease. Three of the patients in this series complained of pruritus of the lower extremities, which was worse during the winter months. There was lichenification of the skin present in one of these patients. The skin of the legs was very dry in these same patients. Considerable relief was afforded in each case by the avoidance of soap and water and local applications of an emollient cream. The patient who had lichenification of the skin in addition to the other findings common to pigmented purpuric disease satisfies the criteria of pigmented purpuric lichenoid dermatitis of Gougerot and Blum. We feel that nothing is added to the understanding of pigmented purpuric disease by subclassifying the cases as Majocchi's disease,

Schamberg's disease, or Gougerot and Blum's disease. None of the patients in this series had red puncta as the sole clinical finding, and so we do not know what the superficial vascular changes are in angioma serpiginosum. Since a purpuric and pigmented phase is not described as part of the clinical manifestations in angioma serpiginosum, it is doubtful that this entity should be included in the same class as pigmented purpuric disease.

Randall et al.[1] reviewed the histopathology of pigmented purpuric disease and felt that the microscopic picture was similar except in degree, there being no characteristic histopathologic feature unique to any one of the conditions. They described endothelial proliferation of the superficial vessels in the papillary and subpapillary regions, resulting in newly formed capillaries. In none of the areas that we studied in the 12 patients by capillary microscopy did we see evidence of new capillary formation. They also postulated that there is frequently a stasis factor playing a role in pathogenesis even in the absence of gross venous incompetency. The lack of any dilatation of the venous subpapillary plexus in early lesions studied by capillary microscopy does not support this contention.

In all 12 of the patients in this study, blood sludging or intravascular clumping of the formed elements was a consistent finding. This phenomenon was not limited only to the vessels of involved areas of skin but was also observed in the nailfold capillaries of each patient. There was no relation between the degree of sludging and the activity of the disease process. The causes of intravascular clumping of the formed elements of blood are many.[5] We have seen sludging in normal persons with no apparent disease. It is commonly present in the vascular bed of skin which is the site of an inflammatory process. Intravascular sludging can be produced in the superficial circulation of the skin by the application of a tourniquet to an extremity, and it is usually found in the vascular bed of the skin of patients with stasis due to congestive heart failure. Knisely[5] has found that drugs and any febrile illness may result in intravascular sludging. He has postulated that sludging may produce pathologic alterations in tissue by causing minute thromboses. It is a possibility that sludging plays a role in the pathogenesis of pigmented purpuric disease. The passage of a clump of cells through an end-capillary can be seen to interrupt the usual laminar flow and greatly retard the rate of flow through the vessel. The large clump of cells in moving through the narrow end-capillary may mechanically damage the lining of the vessel. Some other factor, as yet unknown, must be present before sludging can be perceived to produce a persistent anatomical alteration in capillaries, because the majority of conditions in which sludging has been described are not associated with purpuric eruptions of the skin.

The criteria for classifying a purpuric disease as a vascular purpura include the demonstration of a normal clotting mechanism and normal platelet function. Bleeding results from intrinsic or extrinsic abnormalities of the vascular bed itself. An example of vascular purpura with intrinsic vascular change is hereditary telangiectasia. In this disease, anatomically abnormal vascular structures from which bleeding occurs are present in the skin. The Ehlers-Danlos syndrome and purpura senilis are examples of the vascular purpura group in which the extrinsic factors of an altered stromal support of the superficial vascular bed contributes to bleeding in the skin. Pigmented purpuric disease is classified with the vascular purpuras because there is an absence of clotting defects, normal platelet function is present, and a consistent anatomical defect in the superficial capillaries of the skin is demonstrable.

Only 2 of the 12 patients in the series had a positive tourniquet test, and this is a somewhat lower incidence than has been reported previously.[1] There was no other discernible difference between these two

patients and the remainder of the group. The number of patients with a positive tourniquet test might have been increased had the tourniquet been left on longer.

The aneurysmal dilatation in the end-capillaries is the intrinsic anatomical defect in pigmented purpuric disease, and the marked perivascular cellular infiltrate probably operates as an extrinsic factor contributing to the fragility of these vessels. It is not known whether the cellular infiltrate precedes development of the initial capillary changes in pigmented purpuric disease.

One patient with pigmented purpuric disease also had polycythemia. This association has previously been reported by Gottron[3] and Weiner,[4] who state that the increased viscosity of the blood, the large blood volume, the high platelet count, and high blood pressure often found in the polycythemic patient favor the development of a variety of vascular disturbances.

Recently, Fainshtein,[6] investigating the vascular factor in the development of hemorrhage in aplastic and hypoplastic anemias, has studied the capillaroscopic picture in the nailfolds of 33 patients. Among his findings were dilatation of the capillaries particularly affecting the transitional bends of the vessels and a rapid granular flow. He also found these changes reversible in the hypoplastic anemias during remission following treatment. However, the aneurysmal dilatation of the capillary domes seen by Fainshtein appeared only after the production of venous stasis by means of a cuff applied to the extremity. The transitory dilatation of the transitional or dome portion of capillaries described by Fainshtein and the persistent aneurysmal dilatation of the dome portion of the end-capillaries we found in our patients focuses attention on the role of this particular part of the superficial vascular bed in diseases with purpuric manifestations. This portion of the capillary appears to be the same histologically as other capillary endothelial tubes. Normally, the diameter of the dome portion of skin capillaries is the same as the venous capillary limb and is somewhat wider than the arterial capillary limb. The most noticeable characteristic of this portion of the end-capillary is its marked curvature. This curvature in the capillary tube may be an important factor in causing this portion of the end-capillary to be more susceptible to damage as a consequence of alterations in the hemodynamics of the capillary blood flow resulting, for example, from intravascular sludging. It appears that investigation of the vascular factors contributing to increased capillary fragility in purpuric diseases might well be fruitful if directed toward study of the dome portion of the superficial capillary and its response to altered capillary hemodynamics.

Summary and Conclusions

The superficial vasculature of the skin in 12 patients with pigmented purpuric disease was examined by capillary microscopy.

An aneurysmal dilatation of the dome portion of many capillaries in involved areas of skin was found, and these dilated vessels appear grossly as red puncta.

The dilated capillary dome is weakened and is the site of petechial hemorrhage. Hemosiderin deposits in the skin follow repeated episodes of bleeding.

Capillary regeneration was not observed, and sites which are repeatedly involved by petechiae eventually are devoid of end-capillaries. Loss of the capillaries eventuates in atrophy of the dermal papillae. At times the venous subpapillary plexus in regions devoid of end-capillaries becomes permanently dilated and may appear through a thin epidermis as telangiectatic vessels.

Intravascular sludging was a consistent finding in all patients and was present in vessels other than those in involved areas. No correlation between the degree of sludging and the activity of the disease was discernible.

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Ehlers-Danlos Syndrome

Correlation of Clinical and Histopathological Findings

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Ehlers-Danlos' syndrome is a dysplasia of the mesenchymal tissue characterized by abnormal hyperlaxity and elasticity of the skin; dermofragility, or easy bruising and splitting of the skin at the slightest provocation, with formation of deep wounds, hematomas, and pseudotumors, and, finally, hyperlaxity of the joints. Tobias [10] and others [8] suggested that the symptoms were manifestations of a generalized mesenchymal anomaly with changes in the connective tissue in skin, tendons, joint capsules, large vessels, and internal structures. Publications based on necropsy findings in Ehlers-Danlos' syndrome have not been found in the literature, and definite proof of a universal mesenchymal anomaly is lacking. Tscherno-Gubow first described the condition in 1892, whereas Ehlers [4] made his report in 1901 and Danlos,[3] in 1908, respectively.

Most cases occur in isolation,[1,3-5,7,8,10,12,17-19] and some authors consider the condition a recessive one. Others, as Wiener [12] and Johnson and Falls,[6] and one of us (K. O. H.[14]) have been able to follow the condition through several generations, and maintain that Ehlers-Danlos' syndrome is inherited as a dominant. Incomplete pictures are frequently seen (formes frustes),[6] and this may easily explain the difference of opinion about the mechanism of transmission. Other authors have described the occurrence of a complete [5] and a partial monosymptomatic case [13]—forme fruste—in the preceding generation. We felt that reporting on eight complete cases occurring in the same family with biopsy results in three was justified as an attempt to clarify the mode of transmission and the microscopic alterations.

Submitted for publication June 14, 1958.

Report of Cases

Studies are presented based on three cases in which histopathologic studies were made, out of the family of eight afflicted by this syndrome. A geneological diagram is also given.

All affected cases listed in Figure 1 exhibited the complete syndrome, with fragility and hyperelasticity of the skin and hyperlaxity of the joints, whereas no investigation for formes frustes in the family was carried out. Biopsy of the skin was performed in the patients 1, 2, and 3 (marked with asterisks in Figure 1).

CASE 1.—A man reported to a military dispensary because of an ankle sprain and because of large traumatic lacerations of the skin over the knees, shins, and hands. At the age of 4 months he and his twin brother (Case 2) had had hemangiomas of the back removed. Further examination at that time revealed an inguinal hernia in the patient, and an umbilical hernia in his twin. The typical story of fragility of the skin dated back to early childhood. Even minor traumata caused deep splitting of the skin, and the wounds showed wide separations which did not bleed more than wounds in anybody else. The healing was relatively rapid in the beginning; then atrophic and hypertrophic processes took place, with formation of pseudotumors and irregular scars. Final healing was delayed to usually two to three times as long as would normally be expected, but complicating infections often further delayed the healing. At a later date the pseudotumors showed a tendency for breaking down with discharge of pus or necrotic material. Sutures tended to cut through, and the patient preferred to tape his ulcers rather than go to a doctor. Furthermore, laxity of the skin was most pronounced and he also had extremely lax joints with frequent distortions in the ankles.

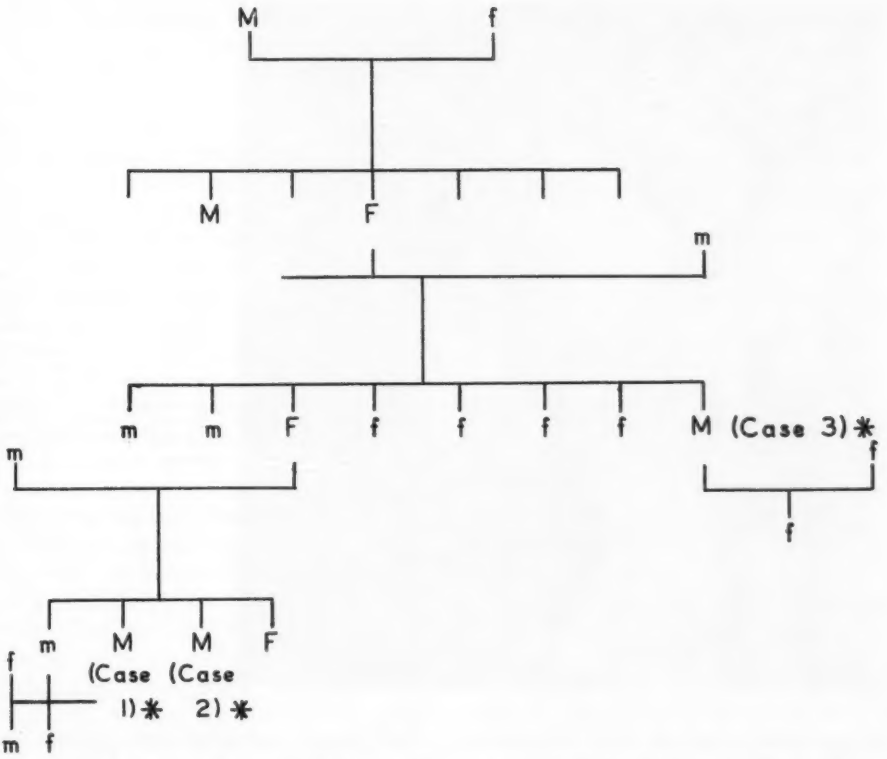


Fig. 1.—Pedigree demonstrating the inheritance of Ehlers-Danlos' syndrome as an autosomal dominant factor. *M*, afflicted male; *m*, nonafflicted male; *F*, afflicted female; *f*, nonafflicted female. Biopsy of the skin was performed in the patients marked with asterisks.

Examination revealed a 21-year-old man of good build and of high intellect, and the typical lesions were distributed as indicated in the photographs. A moderate acrocyanosis was noted on hands and feet, and there were also slight perniotic changes on the posterior aspect of the upper arms. No Raynaud's phenomenon could be elicited. Peripheral pulses were satisfactory.

The skin was lax and could be raised to 2 or 3 in. in height over the forehead, sternum, and elbows, but snapped back in correct position when released. The upper lateral part of the eyelids was lax and hanging down over the limbus. Fingers and toes could be hyperextended, whereas the ankles and shoulder joints showed less changes. The patient felt subjectively well, and no endocrine abnormality was evident. Funduscopy, neurologic examination, and studies for bleeding or coagulation disturbances were all nonrevealing.

Case 2.—The twin brother appeared similar to the previous case but was of a somewhat lighter build. Still, the two were considered to be identical twins. This man was hospitalized in 1945 and in 1951 because of chronic osteomyelitis of the tibia. His complaints otherwise were identical to those listed in Case 1. Biopsy specimens were taken from the leg.

Case 3.—A 34-year-old maternal uncle of the twins was seen in 1951. Complaints were identical to those of the twins, as were body build and clinical features. A biopsy of seemingly "normal" skin over the pectoral muscle was performed.

Other Cases in the Family.—No biopsy specimens could be obtained from the five other affected members of the family, and neither were biopsy specimens obtained from the presumably normal members of the family. The affected male members of the family were noticeably more scarred and deformed than the affected females, which may be related to greater exposure

Fig. 2.—*A*, atrophic, scar-like changes somewhat similar to achrodermatitis chronica on the lower extremities, with a preference for the bony prominences. *B*, scar-like changes with pseudotumors on the forearms. *C*, closer views of the pseudotumors following minor traumas. *D*, increased elasticity of the skin.

to traumata in the male with resulting more wounds and injuries. Joint symptoms were negligible in most instances.

Comment

The pedigree (Fig. 1) for our cases is highly suggestive of an autosomal dominant factor as transmitter of the disease, and similar reports have appeared in the literature.[6,11] Other authors have mentioned consanguinity,[6,7,9,11] prematurity,[6] and endocrine disturbances[6,9,16,18] as causes of Ehlers-Danlos' syndrome or as modifying an inherited tendency. Extensive inquiries did not reveal consanguinity or prematurity in our cases. Neither were obvious endocrine disturbances present. Several investigations[6,10] have found a high frequency of congenital abnormalities, and epicanthus, prognathia, microcephalus, mental retardation, absence of abdominal musculature, bradydactylia, and acrocyanosis have been reported. The twins had broad hands with short fingers and acrocyanosis, but no congenital defects were noted.

Hormones, vitamins, and other forms of medicaments have been tried and found unsuccessful unless diseases of deficiency in need of correction existed in the same patient. The only treatment of value is a conscientious local treatment of the wounds with liberal use of general antibiotics, combined with abstinence from exercises promoting injuries. The genetic prophylaxis must be considered important inasmuch as inbreeding or marriage between two persons with symptoms of this syndrome in complete or incomplete forms may give rise to the occurrence of a double dose of genes in the offspring.

Histopathology

There is no uniform agreement as to the histopathological findings in Ehlers-Danlos' syndrome. For this reason, we feel that it is worth while to discuss the histopathology in the three cases presented in some detail.

The clinical findings are typical, and the family history is unusual in the many members afflicted with the disease. It would seem reasonable to consider the pathology found in the skin sections as fairly typical of the disease, as they all show the same changes, with variations in degree only. Our findings are in agreement with those stated by Ormsby and Montgomery.[15]

Ormsby and Montgomery state in their textbook that all authors agree that there is an increase in elastic tissue. There are, however, exceptions to this, and Brown and Stock,[1] Haxthausen,[5] and also Strandberg[9] found a decrease. Ronchese[7] and Tobias,[10] on the other hand, mention an increase. These authors are in agreement, however, in stressing a somewhat atrophic epidermis with plentiful, loose subcutaneous tissue and a relative decrease in collagenous fibers. Lewitus[16] does not discuss the histopathology in his case, but the photomicrograph shown in his publication demonstrates mainly loose collagen bundles and swollen, fragmented elastic fibers. Bettman[18] mentions the remarkable absence of elastic fibers in his case. The fibers present were distorted and fragmented, while there was normal quantity of the collagen connective tissue of the corium. The vessels showed the same changes, and at later autopsy all organs were found to be characterized by the same disorder of the connective tissue. According to Ormsby and Montgomery,[15] Satenstein stresses the most marked increase of the elastic tissue to be present in the upper part of the corium, and the same text cites Gans as having found changes of elastic fibers to elacin. Montgomery[15] mentions a case of his own with the increase in the elastic fibers and also an apparent merging of the elastic and connective tissue fibers similar to that seen in senile skin and a tendency towards a slight bluish staining of the elastic fibers with hematoxylin and eosin similar to that seen in pseudoxanthoma elasticum. The section also showed marked atrophy of the cutis, with disappearance of most of the collagenous fibers and many dilated blood vessels.

The pseudotumors and subcutaneous nodules described in Ehlers-Danlos' syndrome would appear to vary from small lobules of fat, which Weber and Aitkin[17] called "spherules," to true fibromas of various consistencies with or without a foreign-body reaction (Ronchese[7]). The spherules are also described by Tobias.[10] Studies with the electron microscope have been done by investigators who found the shape of the isolated elastic fibers to be normal when viewed both by the ordinary and the electron microscope. They found the elastic content of the skin of patients with Ehlers-Danlos' syndrome to be about normal.

The biopsy material in the present studies includes four specimens taken from three patients with Ehlers-Danlos' syndrome—all members of the same family and all men. Details are given in the Table. The important findings would seem to be the following: The histopathology of Ehlers-Danlos' syndrome is characterized by an increase in elastic fibers and also qualitative changes in elastic and collagenous tissue. There is an increase in elastic tissue most marked in the upper corium, which may be an evenly distributed increase or may occur in areas. In addition, there is swelling and fragmentation, most pronounced in the deeper layers. The changes in the elastic tissue also involve the vessels with increased elastic tissue and fibrosis. There is no significant reduction in collagenous tissue, but there is looseness of collagen fibers and evidence of merging with the elastic fibers. Epidermal cysts are present in two of the biopsy specimens, and as far as we have been able to find this represents a new feature which we would consider compatible with the easily traumatized skin in Ehlers-Danlos' syndrome. A foreign-body reaction is present in one specimen, but "spherules" are not seen. Epidermal findings are not significant except in showing hyperkeratosis rather than atrophy. Three different stains

Ehlers-Danlos' Syndrome

Case	Site	Epidermis	Elastic Tissue	Collagen	Corium	Vessels
1	Dorsum of hand	Hyperkeratosis, increased granular layer, mild acanthosis	Increased amount in upper cutis; fragmentation & clumping & swelling in lower cutis	Degeneration & clumping	Perivascular, chronic infiltration; foreign-body reaction; epidermal cyst	Increased number & thickened walls
1	Dorsum of hand	Hyperkeratosis, increased granular layer, mild acanthosis	Increase in upper cutis in irregularly distributed areas; clumping, fragmentation & swelling in deeper corium	Mild degeneration & merging with the elastic tissue	Epidermal cyst	Vessels increased in number
1	Lower arm	No remarkable features	Even increase throughout the corium	Slight degeneration		
3	Chest	No remarkable features	Increased amount throughout corium with clumping, swelling & fragmentation in lower cutis	Slight degeneration		
2	Leg	Hyperkeratosis, increased granular layer, mild acanthosis	Increase in upper cutis; clumping, swelling & fragmentation in deeper cutis	Slight degeneration & merging with elastic tissue		Increase in number & thickened walls
2	Leg	Hyperkeratosis, increased granular layer, mild acanthosis	Irregular increase & almost nodular in areas; clumping, swelling & fragmentation in lower cutis	Degeneration & merging with elastic tissue		Increase in number; thickened walls

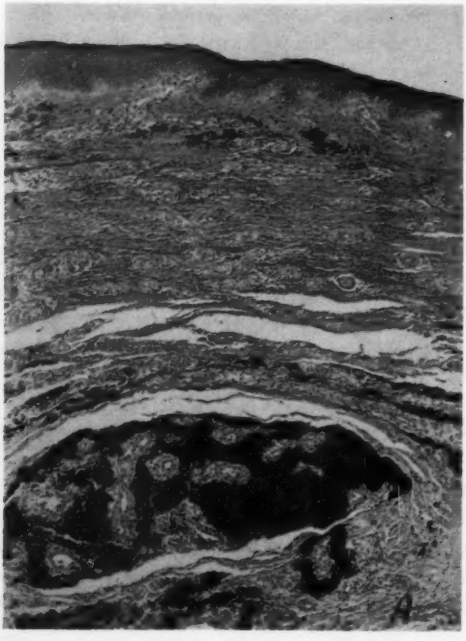


Fig. 3A.—Irregular increase in elastic tissue, with clumping, swelling, and fragmentation. In some areas the elastic tissue forms regular nodules. Elastic tissue stain; × 70.

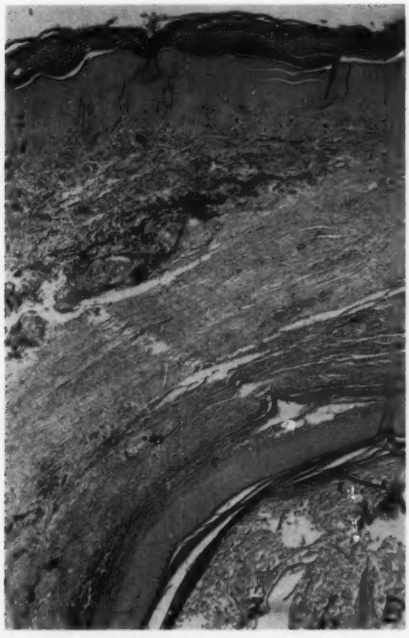


Fig. 3B.—Epidermal cyst. Increased elastic tissue in areas in upper cutis, with fragmentation, clumping, and swelling. Elastic tissue stain; × 30.

were used in preparing the sections: elastin Van Gieson, elastin-Kernechtrot, and hematoxylin-eosin-Masson stain. Of these stains, elastin-Kernechtrot was found to be the best one even if the elastin Van Gieson was satisfactory. The hematoxylin-eosin-Masson stain was found to be of no value in evaluating the slides. This would correspond with Montgomery's result for periodic acid-Schiff (PAS) stain in Ehlers-Danlos' condition.

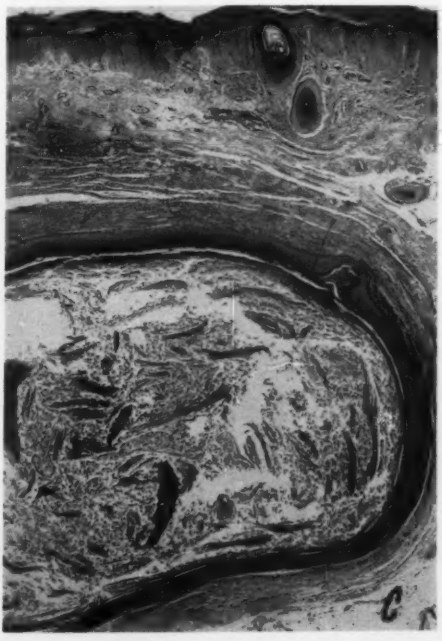
Conclusions

On the basis of studies of biopsy specimens from three patients with Ehlers-Danlos' syndrome in a family with eight known cases, we regard this syndrome as having histopathological findings specific enough to allow a diagnosis. The important findings are an increase in elastic tissue, swelling and fragmentation of the elastic fibers, looseness of the collagenous fibers, and evidence of merging with the elastic fibers. In these findings we are in agreement with the histopathology as stated by various investigators and stressed in the Ormsby-Montgomery [15] textbook. The epidermal changes do not seem significant. The cutaneous vessels may show changes corresponding to the connective tissue otherwise. A new feature presented is the occurrence of epidermal cysts.

Summary

Eight cases of Ehlers-Danlos' syndrome, i. e., hyperelasticity and fragility of the skin combined with hyperlaxity of the joints, occurring in the same family are reported. The pedigree suggests a dominant mechanism of heredity of this disease. Microscopic studies were carried out on skin biopsy specimens from a pair of twins and their maternal uncle. The histopathological picture is considered to be characteristic. A new feature was the occurrence of epidermal cysts. Except for local treatment and liberal use of antibiotics, no treatment can be suggested. Because of the danger of

Fig. 3C.—Epidermal cyst. Van Gieson stain; × 18.



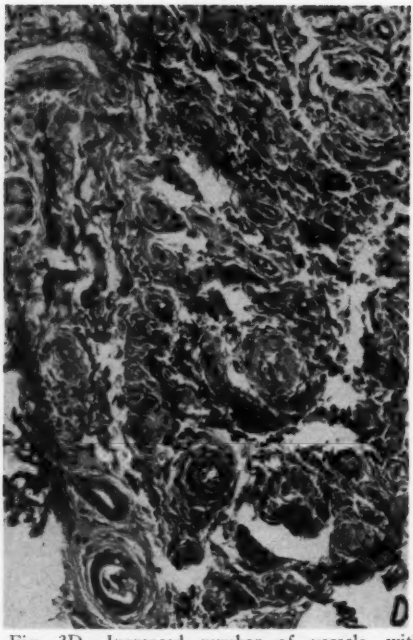


Fig. 3D.—Increased number of vessels, with thickening of vessel walls. Elastic fibers show fragmentation, clumping, and swelling. Elastic tissue stain: × 140.

the occurrence of double genes in the offspring, inbreeding or marriage between patients affected with complete or incomplete manifestations of this syndrome is discouraged.

Dr. Hamilton Montgomery, of the Mayo Clinic, Rochester, Minn., reviewed this paper and the biopsy specimens.

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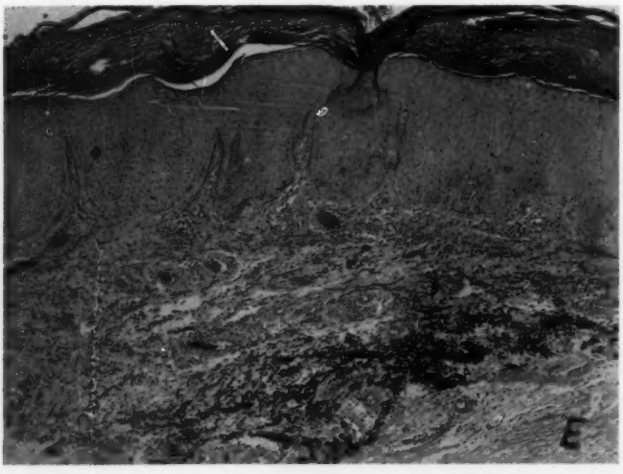

Fig. 3E.—Increase in elastic fibers in upper cutis and clumping, swelling, and fragmentation of elastic fibers in the deeper cutis. Elastic tissue stain; × 60.

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Cicatricial Alopecia and Vitamin A

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Diagnostic determination of diseases of unknown pathogenesis is of necessity vague; great confusion has arisen with regard to the pseudopelade of Brocq and other forms of atrophic permanent alopecias. It has been the fashion of the last century to describe numerous, clinically slightly aberrant, forms as separate entities, while now the general tendency prevails to lump together different clinical disorders on the basis of one common characteristic. This trend is also apparent in the classification of the disorders under discussion. Brocq, in 1888, described a cicatricial patchy atrophy of the scalp as sycosis lupoide, and Unna, Hoffman, Galewsky, and others described the same, or very similar, conditions under different names.* Brocq stressed the absence of clinical inflammation in his cases, which differentiates this disorder from the alopecias due to purulent folliculitis, but Miescher and collaborators and others noted a certain amount of papillary reddening in many instances. Pierini and Borda reported several cases of association of lichen planus and pseudopelade of Brocq and Spier,[1] and others concluded that this disorder was a variant of lichen planus. Degos and coworkers[2] observed 100 cases of patchy atrophic alopecias; 39 of these appeared in the classical form as described by Brocq, while a coincidence with a variety of other skin diseases was noted in the remaining cases. Degos does not consider pseudopelade as an autonomous disease and suggested the term of a "pseudopeladic state."

Follicular keratoses on the border of growing lesions had been noted by many authors; 16% of the patients described by Degos[2] showed some associated keratoses. These follicular keratoses may be minimal and hardly visible or may appear as large horny follicular cones. In 1915 Graham Little[3] described a syndrome consisting of lichen spinulosus of the trunk and cicatricial patchy alopecia of the scalp associated with nonpermanent alopecia of the pubic and axillary hair. Spier and others[1] considered this as a lichen ruber follicularis, a view not shared by Graham Little.[4] A comprehensive and lucid discussion of this problem is found in Guy Prieto's[5] recent article.

Clinical Study

We have observed a number of patients with cicatricial alopecias in whom vitamin A therapy resulted in arrest of progression and in some instances in a limited marginal regrowth of hair.

CASE 1.—This case was a characteristic example of the syndrome described by Graham Little. She was first seen in 1947, at the age of 27 years. She gave the history of a patchy alopecia which started at the age of 13. The patches enlarged steadily, although there were periods when the process appeared to be stationary and others when rapid progression was noted and eventually it came to a coalescence of these patches. On examination a large hairless area extending from the vertex to the forehead was noted. On closer examination it became evident that this large area was composed of several coalescent patches. The center of the patches showed atrophic, shiny, thin skin; on the borders some residual hair and numerous follicular horny plugs were evident. No pustules or signs of active folliculitis were found at any time. The center of the face showed a slight bluish erythema, large pores, and some keratoses; the eyebrows were thin and scanty.

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Department of Medicine, Sub-Department of Dermatology, McGill University.

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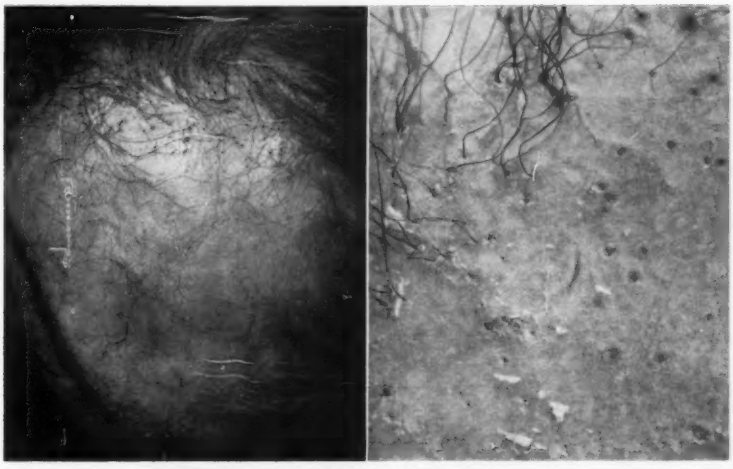
* The references to the older German and French articles may be found in Spier's[1] and Prieto's[5] papers.



Cicatricial alopecia.

Axillary and pubic hair was present but sparse. On chest, back, and particularly on the extensor surfaces of the extremities a typical lichen spinulosus was present, and a mild diffuse bran-like desquamation was noted on arm and legs. No lesions resembling a lichen planus were seen.

Internal examination showed no particular abnormalities; the diet history suggested an adequate vitamin A intake, and the patient had no complaints other than the dry skin, the alopecia, and general tiredness. For the latter she had used vitamin tablets for several months. A hemogram, the basal metabolic rate, and several liver-function tests showed nothing abnormal. The carotene and vitamin A content of the serum was within normal limits at the first examination, but this result was equivocal, since she had taken tablets containing vitamin A during the months preceding the examination. Later examination performed without preceding vitamin A intake showed abnormally low values (36 I. U.).

The histological examination showed no evidence of any cellular infiltration and was not suggestive of a lichen planus. She was then given 150,000 units of vitamin A intake per day, and after six weeks a marked improvement of her condition occurred. The follicular keratoses had disappeared; the hairfall had stopped, and there was a marked regrowth of hair at the borders of the patch where the keratoses had been seen. The follicular lesions on the body had disappeared, and the skin appeared less dry. Vitamin A therapy was continued in a reduced dose for three months, and no further changes occurred for two years. At this time she returned, complaining of renewed alopecia and of dryness of the skin; her serum vitamin A was abnormally low at this point. She was again given vitamin A; the condition improved again, and she has since been maintained by 100,000 units of vitamin A given three times a year for a period of six weeks. She has returned for yearly follow-up examinations, and the condition has remained stationary. She has been followed for 11 years.

CASE 2.—A 25-year-old woman complained of an increasing number of bald patches for three years. She had suffered a total alopecia following typhus at the age of 14, with subsequent complete regrowth of normal hair. Examination showed several small patches of alopecia; her diet was normal. The center of the patches was atrophic with no visible follicles; the margin showed widened follicles, and minimal keratosis could be discerned under the magnifying glass, but there was no erythema or scaling. There was an insignificant follicular keratosis on the shoulders.

The fasting carotene was high; the vitamin A values were low (42 I. U.). When she was given 150,000 units of vitamin A daily, the progression of the process stopped and the keratoses disappeared slowly. After discontinuation of the therapy for several months, a sudden reactivation of the process occurred and the patches increased in size. The patient has since been taking vitamin A regularly three times yearly for a six-week period. For the past six years she has been followed by yearly examinations and the size of the patches has remained unchanged.

CASE 3.—A 32-year-old man gave the history of progressive hairfall for five years and increase of patches during the last months. The onset of the disorder coincided with a violent gastrointestinal upset. Examination revealed numerous atrophic patches on his scalp with small but definite fol-

licular keratoses on the margin. The history was not contributory, but his diet had been low in protein and vitamin A for several years. Both his carotene and vitamin A serum level were low (carotene 10 I. U.; vitamin A 43 I. U.).

Vitamin A medication, 150,000 units a day, resulted in disappearance of the follicular keratoses and complete arrest of progression.

Two more patients with an identical clinical picture showed similar response to vitamin A therapy.

Laboratory Studies

Materials and Methods

The carotene and vitamin A serum levels have been determined fasting and three hours and six hours after ingestion of 200,000 units of vitamin A. The calorimetric method of Carr and Price was used.[6] The following groups were examined.

I. Fifteen healthy volunteers

II. Eight patients suffering from contact dermatitis and other minor skin disorders

III. Five patients with ichthyosis

IV. Five patients with various dematoses involving disturbances of keratin formation

V. Four patients with cicatricial alopecia featuring follicular keratoses.

Results

Only the fasting vitamin A values are recorded, since neither the carotene nor the values after vitamin A medication showed any consistent abnormalities.

The mean values and standard error of the control groups were 86.3±4.6 I. U. and are within the limits of normal described for healthy persons. The first seven values in Group I were those of men (mean and standard error 94.6±6.4 I. U.). Corresponding values for the remaining eight women listed in Group I were 79.0±5.7 I. U. Differences due to sex were on the borderline of significance ($0.01>P>0.05$), the values in males were somewhat higher than those in females.

TABLE 1.—*Fasting Vitamin A Serum Levels (I. U.) in Various Skin Diseases*

Group I	Group II	Group III	Group IV	Group V
81.8	61.0	53.0	83.0	36.0
117.1	58.0	81.0	44.0	32.3
119.4	94.0	60.0	16.3	32.6
92.0	67.0	97.0	22.3	50.0
87.0	46.0	20.4	43.0	
88.0	101.0			
77.0	112.0			
99.3	46.3			
92.0				
78.2				
57.2				
81.1				
63.0				
96.0				
65.0				
86.3±4.6 *	73.2±9.1	62.3±13.0	41.7±11.7	37.7±4.2

* Mean and standard error.

TABLE 2.—*Analysis of Variance of Data in Table 1*

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F	P
Between groups	4	12473.21	3118.30	6.498	<0.001
Within groups (error)	32	15355.86	479.87		
Total	36	27829.07			

An analysis of variance was conducted on the data of the five groups. The difference between the groups being highly significant, the performance of the *t*-test between the various groups utilizing the standard error variance was derived from the error variance was permissible. The following results were obtained:

1. There was no significant difference between the two control groups (Groups I and II, $0.20>P>0.10$).

2. Group I was significantly higher than Group III ($0.05>P>0.02$) and higher than Group IV ($P>0.001$) and Group V ($0.01>P>0.001$).

3. Group II showed significantly higher values than Groups IV and V ($0.05>P>0.02$).

4. All other differences between the Groups were not significant ($P>0.10$).

Werner Jadassohn[8] has rightly pointed out the contradictions and the ambivalence of some of the reports on vitamin A serum levels and on therapeutic results achieved with this vitamin.

Our material suggests that the fasting vitamin A levels are somewhat higher in males than in females. There was no statistically significant difference between control Groups I and II, but some low values were noted in Group II, which in-

cluded patients of a lower socioeconomic status and probably poorer diet as compared with the group of volunteers, all of whom were doctors and nurses. Groups I, II, III, and V had only young persons, while in Group IV three old patients were included. The lowest values were found in a keratotic erythroderma (16.3 I. U.) and in a case of Darrier's disease (22.3 I. U.). The serum levels of the four cases of alopecia with follicular keratosis (Group V) were uniformly low.

Comment

We agree with Degos' concept of a pseudopeladic state and believe with Prieto and others that pseudopelade of Brocq in its atrophic stage is indistinguishable from terminal stages of cicatricial discoid lupus erythematosus or lichen planus, folliculitis decalbans, and other disorders.

Some of the early and progressive cases of these cicatricial alopecias may show marginal follicular keratosis. The low fasting vitamin A values and particularly the therapeutic result achieved with vitamin A therapy suggest that a disturbance of the vitamin A metabolism may be present in these cases.

Summary

Three cases of pseudopelade of Brocq, showing marginal follicular keratosis, and one case of Graham Little syndrome were treated with vitamin A, with the result that the progress of the disease was arrested. The fasting serum vitamin A levels of these four patients were determined and compared with those of normal subjects and were found to be significantly lower than the values of the control groups; the absorption of vitamin A after oral medication appeared to be normal.

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Destruction of Fingerprint Pattern by Superficial Late Syphiloderm

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The subject of this report is the unusual occurrence of a syphiloderm on the palmar aspect of one hand that healed with destructive alteration in the ridged surface pattern of the epidermis and obliterated the identifying features of the fingerprints.

Report of a Case

A 40-year-old white obese woman complained of an extremely pruritic eruption confined to the palm of her right hand. She said that the eruption first appeared when she was 6 years of age and took the form of itchy "water blisters." She had been treated through the years with a variety of local medications, but there was never complete healing.

The patient was examined on Feb. 10, 1945, and presented a diffuse, dull erythema with scattered areas of crust formation and exfoliation over the complete palmar aspect of the right hand and accentuated wrinkling over the fingers and thenar region. The involved part was delimited from the normal skin by a gyrate and slightly infiltrated border at the volar wrist, with extension there along both the medial and the lateral aspects of the hand. The remainder of the skin examination was noncontributory.

Examination of scales from the palm for fungus elements (direct potassium hydroxide mount) was negative. The serologic test for syphilis (Kahn) was reported to be positive, 4+.

Sections of a biopsy specimen removed from the infiltrated border (wrist) on Feb. 17, 1945, were described as follows: "The epidermis is acanthotic with uneven elongation of the rete ridges, partial loss of the granular layer, and dense parakeratotic scales containing microabscesses. The papillae are long and somewhat edematous. A predominantly lymphocytic infiltrate is present in the pars papillaris and intermingling extensively with the epidermal cells of the rete ridges. An accumulation of polymorphonuclear cells is present in the suprapapillary plate. The deeper layers of the corium are free of pathologic changes."

The patient was started on a 10% solution of potassium iodide by mouth on Feb. 17, 1945. The dosage was increased daily, thereafter, until a maintenance dose of 4.5 gm. of potassium iodide per day was achieved.

The skin continued to improve slowly and the gyrate borders disappeared by April 21, 1945. At that time, the potassium iodide was discon-

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Fig. 1.—Palmar aspect of the right hand, showing areas of crust formation and exfoliation with accentuated wrinkling over the fingers and thenar region. Sharp delineation of pathologic process from the uninvolved skin is noted at the palm-wrist junction.

Fig. 2.—Dorsum of right hand, with sharp infiltrated border running along the lateral aspect of hand and proximal thumb.

tinued and bismuth subsalicylate (1.5 cc.) was administered intramuscularly at weekly intervals. The skin was recorded as entirely clear on June 2, 1945. However, on close examination of the right hand, a diffuse dissolution of the normal epidermal ridge pattern of the fingers and palm into rather irregular short lines and dots was noted. Fingerprint impressions were taken of all digits of both

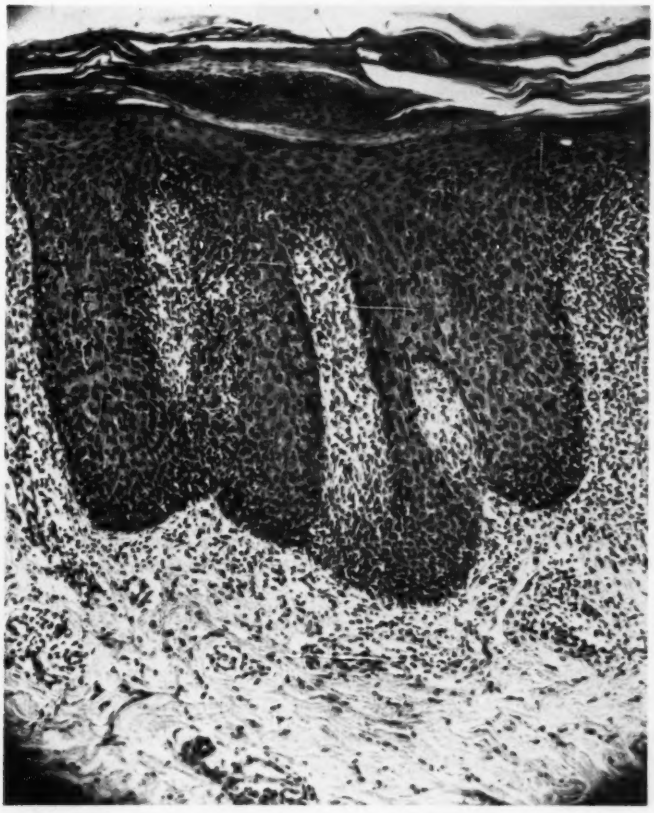

Fig. 3.—Photomicrograph of biopsy specimen from infiltrated border (wrist), showing the extensive inflammatory infiltrate in the superficial corium with invasion of rete ridges. The deeper layers of the cutis are free of pathologic changes; × 135.

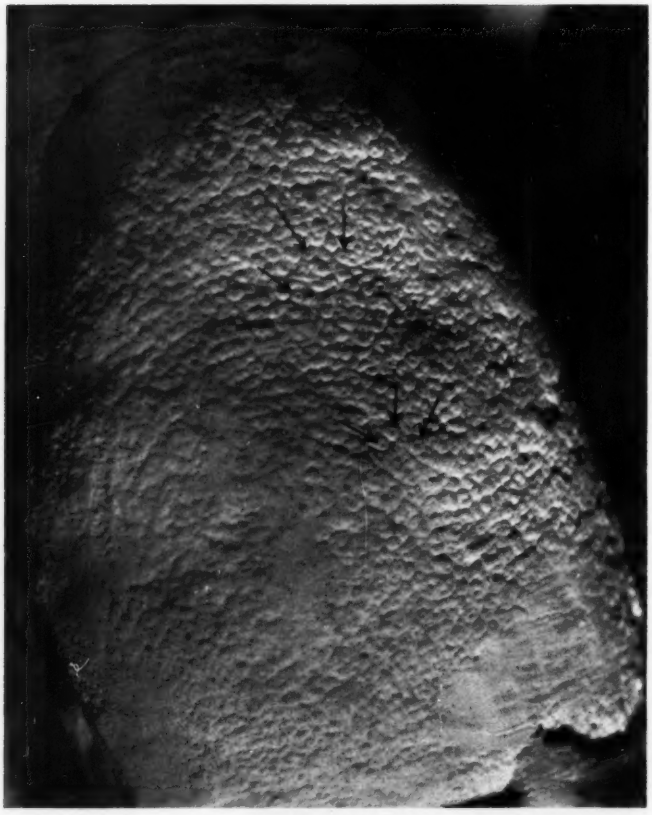

Fig. 4.—Positive cast of the right index finger tip (after treatment) demonstrates dissolution of the normal epidermal ridge pattern by the scarring process. Arrows point to examples of preserved sweat ducts and their respective pores. Reduced 28% from mag. × 10.

hands. The left hand prints were complete in every detail. On the right hand, however, the epidermal ridge formations were destroyed to the point where the general pattern type could not be ascertained with any degree of accuracy.

For a lasting record a mold of Negocoll plastic was made of the fingers of both hands and their negative impression was transferred to fresh plaster of Paris to produce a permanent positive cast.

A repeat Kahn test on June 29, 1945, was reported as positive. The patient's husband had a negative serologic test for syphilis. The couple had no children.

The bismuth subsalicylate injections were continued at weekly intervals until Sept. 28, 1945, after which time the patient failed to return for further treatment. She died about two years later of complications following extirpation of the gall bladder. No autopsy was performed.

Comment

The clinical picture of late syphilis of the skin is characterized by lesions which are sparse, indolent, and asymmetric. An indurated cord-like arciform border with atrophic changes occurring centrally as the border advances is frequently described as characteristic of late syphiloderms.[1] These points are significant in differentiating syphilis from psoriasis, eczema, drug eruption, and dermatophytosis.

Late palmar and plantar syphilids often appear without any other manifestations of late syphilis, and as a rule only one palm or sole is affected.[2] The advancing border may spread to involve the palmar and plantar aspects of the fingers and toes, but it rarely attacks the dorsal aspect of the hands or feet.[3] Morphologically, the lesions may be either (*a*) single and psoriasiform in type, (*b*) multiple, small, scaly and polycyclic, or (*c*) multiple, keratotic, and punctate with plugs and pits.[4]

Although the presence of vesicles eliminates syphilis for all practical diagnostic purposes, a syphilid of the palm may be coincident with an eczematous dermatitis, thereby confusing the clinical picture.[2]

In this patient, it may be assumed that she had acquired a dermatitis of her hand in childhood which served as a locus minoris resistentiae and favored localization of the late syphiloderm. No accurate history of the syphilitic infection was obtainable.

Permanent destruction of the fingerprint pattern in healed late syphilis of the palm is rare. Survey of the literature disclosed that Vieira [5] described a case of late syphilis which caused destruction of the epidermal cristae (ridges) of all fingers of one hand, as in the case reported by us. In contrast, fingerprint changes with permanent alteration of the epidermal ridges are not infrequently observed in leprosy.[5]

Alteration in the fingerprint pattern in our case was due to irregular destruction of the epidermal cristae, giving both a broken line and a beaded appearance. The terminal portion of the sweat ducts, the only superficial structures not involved, kept up some semblance of ridge formations.

Cutaneous elevations which characterize late syphilids of the finger tips are due to cellular infiltrates in the pars reticularis of the corium. When these granulomas heal, scar formation ordinarily takes place in this portion of the cutis; the pars papillaris and the overlying epidermis are only mildly involved by secondary atrophic changes.

We have previously reported that accurate reproduction of the fingerprint is possible as long as the dermal papillae are preserved in their respective double columns.[6] Burks [7] showed that when a major portion of the dermal layer is destroyed the finger heals with a smooth scar, free of any identifying ridge pattern. The usual absence of alteration of the fingerprints in syphilis suggests that scarring of the deeper corium without destruction of the papillary layer does not necessarily affect the ridge pattern.

What makes the pathology in our case different is the unusually superficial cellular infiltrate in the upper corium which actually hugs and sometimes invades the basal layer and rete ridges in many areas. On healing the scar formation must have destroyed the papillary portion of the cutis. It seems, therefore, that the papillary portion is primarily responsible for the reproduction and maintenance of fingerprint characteristics.

An interesting observation in this case is that the terminal sweat ducts appear to have remained unaltered in spite of the pathologic changes surrounding them. Investigative studies on the eccrine sweat gland apparatus have demonstrated that the intraepidermal portion of the sweat duct is a definite structure, independent of the epidermis through which it travels.[8] Lobitz and associates [9] showed that the "epidermal eccrine sweat duct unit" possesses its own highly specialized luminal cells and periductal sheath of epidermal cells. The contraction of scar tissue, which both shrank and distorted the epidermis, spared the epidermal sweat ducts, a fact supporting the concept of its independent stature.

We are fully aware that neither the clinical nor the histologic or fingerprint disturbances of this case are typical of syphilis of the palm. The sharp infiltrated margin of the affected area was the one feature arousing clinical suspicion. The positive serologic tests were supportive, and the prompt, complete, and permanent clearing of the recalcitrant dermatosis under antisyphilitic therapy constituted empirical proof of the diagnosis. The severe pruritus and diffuse involvement of the entire palmar surface of the hand and fingers were misleading. Even the histologic picture simulated psoriasis and certainly was not typical of late syphilis.

This case was presented to the Clinico-Pathologic Conference, American Academy of Dermatology and Syphilology, Chicago, Dec. 7, 1955. Dr. Hamilton Montgomery, one of the panelists reviewing the case remarked: "I agree to a diagnosis of psoriatic syphiloderm. As a neo-

phyte in 1922, I insisted on a histologic diagnosis of psoriasis in a biopsy from a unilateral group of lesions on one arm which Dr. Ormsby correctly maintained were those of a nodular syphiloderm and which responded promptly to treatment."

At this time, a statement by Cabot [10] seems to be most apropos: "In almost every carefully studied case there are one or two facts which stray across the clinical field quite wild and untamed, and never submit to any rational explanation."

Summary

An unusual case of superficial late syphilis of the palm with permanent alteration of the fingerprint pattern in all digits of that hand is reported. The probable mechanisms for the fingerprint changes are discussed.

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The Prognosis of Localized Scleroderma

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While much interest has been given to the generalized systemic forms of scleroderma, relatively little information has appeared about localized scleroderma. Reports concerning the use of various therapeutic agents in localized scleroderma continue to appear, but with a limited knowledge of the natural course of the untreated disease and often a lack of control observations any true evaluation of therapeutic effectiveness or failure can only be presumptive. Dowling [1] has stated, ". . . at present, there is not very much that one can usefully say about it."

In an effort to obtain some information regarding the prognosis in treated and untreated patients, we have summarized the records of 115 patients who had localized scleroderma and who were observed at the University Hospital (Michigan) between 1932 and 1955. It is generally assumed that the disease is self-limited and without serious complications. Much of the evidence for the benign character of localized scleroderma seems to be based upon individual case evaluation rather than a prolonged follow-up in a large series of patients.

Many sources place little stress upon a separation of localized scleroderma into distinct types and the variation in prognosis associated with each type. Since confusion in the use of terms pertaining to localized scleroderma exists, it seems proper to begin this discussion with a definition of the types of localized scleroderma as used in this evaluation. Three clinical forms of localized scleroderma are of definite enough morphologic variations to warrant subclassification.

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Localized Scleroderma

1. *Morphea.*—Morphea is usually characterized by a discrete oval lesion with a firm ivory-colored center and a surrounding violaceous halo. The lesions are usually single or few in number and may vary in size from 1 to 20 or 30 cm. Although the lesion is firm and may be slightly elevated, it is not bound to the deeper structures. Upon involution, it frequently leaves an atrophic area with a decrease or increase in skin pigmentation.

2. *Guttate Morphea.*—This seems to be a variant of the above, but, instead of a few lesions, many small lesions of a white to ivory color are found. The upper trunk and thighs are most frequently involved, but the remaining areas of the extremities and even the face may be involved. A great deal of confusion exists between this entity and lichen sclerosus et atrophicus. Montgomery and Hill [2] feel that microscopic differentiation can be made. These smaller discrete lesions usually do not have the firm sclerodermatous character of morphea.

3. *Linear Scleroderma.*—As is indicated by its name, this form of localized scleroderma is arranged in a band-like linear distribution. It may occur on the head, trunk, or extremities. Its most characteristic point of separation from morphea, in addition to its distribution, is its deeper involvement with fixation to underlying structures. Since its onset is most often during the first two decades of life, its deep involvement of the skin and periosteum may lead to deformities of an extremity or a side of the face. A

history of preceding trauma is frequently obtained. When it involves the face and scalp, it enjoys the term "en coup de sabre."

History

Erasmus Wilson is credited by Fox [3] as the first to use the term morphea, because he felt the areas were vestiges of true leprosy. However, several cases at Guy's Hospital were called white tubercle or morphea previous to Wilson's report. In 1868, Hilton Fagge [4] wrote an extensive essay "On Keloid, Scleriasis, and Morphoea." He clearly delineated the keloid of Alibert (true keloid) from that of Addison (morphea), and pointed out the relation of Addison's keloid to scleroderma. Through a series of case reports he classified the recognizable forms of localized scleroderma. The good prognosis of keloid of Addison was noted, and the atrophy or hemiatrophy associated with linear, or "coup de sabre," scleroderma was recognized. In one case, Fagge pointed out the occurrence of an isolated patch of scleroderma for a two-year period with eventual wasting contractures of the arms and legs.

The observation that an occasional case of localized scleroderma eventuated in a generalized systemic sclerosis prompted interest in this report. Duckworth [5] reported a patient with localized scleroderma followed in five years by weakness, malaise, and joint pains. Much more recently, Leinwand [6] and coworkers reported gastrointestinal changes of generalized systemic sclerosis in a person with typical lesions of circumscribed scleroderma.

Sellei [7] states that morphea may be joined by every form of scleroderma except acrosclerosis. In contrast to these observations, Rothman [8] stated that localized scleroderma is a relatively benign condition without a tendency toward generalized involvement. O'Leary and Nomland,[9] after reviewing 55 cases of localized scleroderma, stated that the prognosis in the condition is good, with nothing to indicate serious or severe constitutional symptoms. Piper and Helwig [10] observed 27 cases of localized scleroderma without evidence of systemic change at autopsy.

Etiology

The etiology of all forms of scleroderma is unknown. Various hypotheses regarding etiology have produced changes in the therapeutic approach. These vogues in therapy were apparent in the evaluation of our series. Trauma has been associated with linear scleroderma. Many individual case reports have given at least clinical support to this impression (O'Leary and Nomland,[9] Boardman,[11] Osborne [12]). Only 10 of our 115 cases gave a history of trauma, 8 of which occurred in linear scleroderma. A true correlation of the injury to the onset of the disease was difficult to ascertain in some instances but seemed definite in others. Thirteen cases of linear scleroderma were reported by Rubin.[13] He felt that a significant number of these cases with involvement in the lower extremities were found to have spina bifida occulta or other minor abnormalities. By careful observation of the pattern of distribution, he concluded that the lesions lie in the long axis of the spinal root zone and less frequently follow distribution of the peripheral nerves. However, Christianson and co-workers [14] found 32 patients with localized scleroderma and congenital abnormalities of the spine in whom the sclerodermatous lesions were frequently proximal to the anomaly and not distal. It was their belief that the same factor or influence is responsible for both the spinal abnormalities and the scleroderma—one congenital, the other latent. In our series only three examples of congenital spinal defects were found. These were all in cases of linear scleroderma. Since x-rays were only obtained in a total of eight persons with linear scleroderma, this low figure may not be significant. Various endocrine changes have been implicated in the etiology of either localized or generalized scleroderma (Castle).[15] No real proof has been offered to

support this. As each gland of internal secretion was considered, therapeutic regimens were altered accordingly. Empirical administration of thyroid was tried, as have been pituitary extracts and heavy metals. Parathyroidectomy (Bernheim)[16] has been recommended, and an interesting observation from our own series will be made later regarding this procedure.

Limited autopsy reports have offered little additional constructive information. Archambault[17] quoted Mende, who found a "proliferative interstitial neuritis" in the peripheral divisions of the trigeminal nerve in a patient with progressive facial atrophy. "Changes" were also noted in the Gasserian, sphenopalatine, otic, and ciliary ganglia. Osborne[12] reported a series of cases with hemiatrophy of the face in association with morphea rather than linear scleroderma. At autopsy, one of these cases had changes suggestive of an old inflammatory process in the motor area of the brain. In our series an autopsy was done on a 4-year-old girl with an "en coup de sabre" type of linear scleroderma on the left. The child had a convulsive disorder and clinical diagnosis of an optic tumor. A "neurocytoma" of the left optic nerve, with hemorrhage into the right lateral ventricle, and a chronic adhesive arachnoiditis in the left frontal, temporal, and occipital areas were found at autopsy.

Haxthausen[18] extended his experimental series of exchange transplants or grafts to include localized scleroderma. He observed that normal skin transplanted to an area of scleroderma took on the features of this process in several months. The reverse was true for sclerodermic skin transplanted to normal areas. The skin assumed a more normal texture. Following transplantation of an area of scleroderma by a pedicle flap, Comel[19] noted the sclerodermic patch to increase in size.

Histochemical techniques have been used to clarify the etiology of localized scleroderma. Musso[20] divided the pathogenic changes of morphea into four stages: (1) fibrillation of collagen-ground substance masses, (2) fusion and eosinophilic change in the collagen ground substance masses, (3) formation of young collagen between collagen-ground substance masses, and (4) areas of connective tissue formation which resemble hyalin degeneration and stain uniformly eosinophilic. Therefore, he feels that the changes in morphea are due to excessive production of normal ground substance and fine collagen fibers. It is interesting to note that Musso made no mention of blood vessel changes in his study. O'Leary, Montgomery, and Ragsdale[21] evaluated the histiologic picture in over 200 cases of scleroderma. Although there were dermatohistopathologic differences that varied with the type and stage of scleroderma, they were not diagnostic. They failed to demonstrate any increase in mucopolysaccharides in any form of scleroderma, with use of the periodic acid-Schiff stain.

It is readily seen that the etiology of localized scleroderma is still unknown.

Comment

Because confusion exists in the classification of scleroderma, not only were case records of localized scleroderma reviewed, but records of generalized scleroderma, hemiatrophy of the head or body, and lichen sclerosus et atrophicus were also examined. Some cases of diagnosed hemiatrophy had sclerodermatous skin changes, while in other cases of hemiatrophy, the skin overlying the atrophic deeper structures was quite normal. These cases of hemiatrophy with sclerodermatous skin changes were included in this report with linear scleroderma. One case clinically interpreted as lichen sclerosus et atrophicus was subsequently diagnosed as guttate morphea on pathological examination, with use of the criteria of Montgomery and Hill.[2] All case histories of generalized scleroderma were reviewed for evidence of the presence of localized scleroderma previous to the onset of a generalized process.

On the basis of the above considerations, 115 cases of localized scleroderma were reviewed. Many of these patients had been

followed in the University Hospital for prolonged periods of time. Regardless, all patients were sent a questionnaire regarding the progress of their disease, and inquiry was made about any type of generalized symptoms, such as joint pains, pain in toes and fingers on cold exposure, difficulty in swallowing. If any symptoms or signs suggested a generalized disease, these patients were recalled and examined.

As might be expected with a group of this size, follow-up was difficult in many cases. However, 111 of the total number (96.5%) were either examined and/or responded to the questionnaire. Two patients had died from other causes without any evaluation of their scleroderma, and the questionnaire response from three patients was too inadequate to be of value in this study. Hence, the course of localized scleroderma in a total of 106 patients was considered in this report. This total includes 60 cases of morphea, 13 cases of guttate morphea, and 33 cases of linear scleroderma. O'Leary and Nomland,[9] in their report of 55 cases of localized scleroderma, had 38 cases of morphea, 3 cases of guttate morphea, and 14 cases of linear scleroderma. This distribution corresponds closely to our own series. Christianson and associates [14] reported a clinical study of 235 cases of localized scleroderma. However, since they divided their patients into two groups—(1) 191 cases with linear lesions or localized sclerodermatous patches and (2) 44 cases with bilateral disseminated symmetric plaques—a comparison was not feasible. An incidence of occurrence in a ratio of at least 2:1, female to male, was noted. Only one case of localized scleroderma occurred in a Negro. This was an isolated area of morphea in a 50-year-old woman. The diagnosis was substantiated by biopsy. Tauber and Goldman [22] mention the absence of hemiatrophy in Negroes. Leinwand and co-workers [6] reported 150 cases of localized and generalized scleroderma, of which only 3 were in Negroes. However, they failed to mention whether these cases had local or systemic involvement. Christianson and associates [14] also failed to mention whether any members of their large series were Negro. It is our impression that localized scleroderma is significantly rare in this race.

The greatest number of patients have been observed over 10 years. Unfortunately, biopsy specimens were obtained in only 28 of the total number of cases followed; 23 were considered to be compatible with a diagnosis of scleroderma. The other five were not specific, but the clinical impression was clearly that of localized scleroderma. We noted that morphea and guttate morphea have no strict age occurrence. In linear scleroderma, however, a great majority of cases occur in the first and second decades. This agrees with O'Leary's [9] report and is borne out by an average age at the time of diagnosis of 12.4 years.

All records were carefully reviewed to determine whether any other conditions or diseases were associated in significant regularity with localized scleroderma. Such an evaluation is difficult, and it was not felt that any correlation could be established. Upon consideration of the distribution of the lesions, it was noted that a majority of lesions in linear scleroderma and morphea were unilateral, while guttate morphea was more frequently bilateral. Morphea more frequently involved the trunk. Linear scleroderma involved the upper and lower extremities about equally.

Prognosis

A general summary of prognosis, regardless of the absence of type of treatment, is presented. In those patients who had morphea, guttate morphea, and/or linear scleroderma of an extremity, over half the cases had lesions which had disappeared or softened, leaving either depigmented or hyperpigmented areas. This was not true of the "coup de sabre" type of scleroderma, in which over half of the patients had lesions which had remained unchanged or become more extensive. Examples of all types of localized scleroderma were noted to involute completely. A most interesting observation

in this series is that four patients with morphea, one with guttate morphea, and one with linear scleroderma were associated with subsequent formation of a true generalized type of scleroderma.

The observation of others that a patient with localized scleroderma may subsequently develop a generalized sclerodermatous process was mentioned earlier. Our observations confirm Fagge's [4] original one that generalized scleroderma may begin as a localized process. Contrary to Sellei's [7] conviction that morphea may be joined by every form of scleroderma except acrosclerosis, a majority of our patients with generalization had Raynaud's phenomenon and slowly progressing sclerodactylia as a prominent part of their symptom complex. Christianson and co-workers [14] also mention two patients with generalized morphea which eventuated into a generalized scleroderma. From our study it would appear that any type of localized scleroderma may be associated with a generalized scleroderma or acrosclerosis. The observation of this progression in 6 cases out of a total of 106 cases is a significant finding.

Therapy

Since the etiology of scleroderma remains obscure, many of the therapeutic approaches have been based on empiricism. The success or failure of any given agent has been formulated after observation of a small number of cases without adequate control. The natural history of untreated localized scleroderma is not well known; therefore, evaluation of any therapy must be equally vague. No attempt was made to compare prognosis in treated and untreated localized scleroderma, but in a total of 60 patients with morphea, 30 had no therapy. If the four patients who had morphea which became a generalized systemic disease are excluded, the over-all prognosis of treated or untreated morphea was essentially the same. It was felt that perhaps the disease in those patients not treated was of less severity than in those receiving therapy. A careful review of the records showed this to be untrue, and that the selection of a therapeutic program was based more upon the chronological popularity of a drug than the severity of the disease. The number of untreated patients with guttate morphea was also about one-half of the total observed. Again, with the exception of the patient that developed a generalized disease, the prognosis of treated or untreated guttate morphea was about the same. However, this was not true for linear scleroderma. The percentage of patients who had received some form of therapy was much greater, and this therapy was frequently surgical.

A variety of surgical procedures was used for the various manifestations and complications of localized scleroderma. Surgery was most frequently used in linear scleroderma. Three patients who had linear scleroderma involving the extremities had regional sympathectomies performed. No improvement was noted. Two patients with "en coupe de sabre" type of scleroderma were treated by plastic repair of the resultant deformity with facia lata and dermal grafts. One of these patients was observed 5 years and the other 10 years, with cosmetic improvement in both. Kazanjian and Sturgis [23] reported similar observations. They found that slow absorption of facial grafts occurred and that dermal grafts were less rapidly absorbed. Longacre and Wagner [24] reported a patient who had linear scleroderma in a lower extremity in which atrophy, flexion deformity, and shortening had occurred. Through the use of a cross leg flap and excision of the atrophic sclerodermatous scar, good functional and cosmetic improvement resulted. This improvement was still apparent six years after the procedure. Since replacement of the involved soft tissue was accompanied by a cessation of the bony deformity, it may support the impression that the bony changes occurring with linear scleroderma are secondary and not primary to the soft tissue involvement. Perhaps the most remarkable surgical approach and result was observed in one of our patients. He clearly had a progressive systemic disease and was given a poor

clinical prognosis. Several weeks after a subtotal parathyroidectomy, excellent improvement resulted, but he was not again examined until the present study. His skin now is normal except for some atrophic patches in the anterior tibial areas. In 1937 Leriche and co-workers [25] observed 13 persons with generalized scleroderma for two to five years after a subtotal parathyroidectomy with 90% improvement. The rationale of this procedure was based on three factors: 1. An injection of parathormone into rats produced skin changes similar to scleroderma. 2. Calcium deposition in soft tissues frequently occurred in scleroderma. 3. Decalcification of bone was a frequent finding in scleroderma. In 1939 Bernheim and Garlock [16] reported improvement in 12 of 13 cases with generalized scleroderma following subtotal parathyroidectomy. However, their observations were only for a two-month to three-year period. More recent reports have not appeared in the English literature to support these observations, and the procedure has fallen into disuse for the treatment of generalized scleroderma.

Summary

Over 75% of 106 patients who had localized scleroderma were observed for a period longer than five years. Localized scleroderma occurs in three rather specific morphologic types: morphea (60 cases), guttate morphea (13 cases), and linear scleroderma (33 cases). The etiology of this group of diseases is still unknown. In general, a large percentage of these patients improve spontaneously; however, linear scleroderma has a greater tendency toward progression. Linear scleroderma occurs primarily in the first two decades. This is not true of morphea or guttate morphea. In all types, the female is affected more frequently than the male. The occurrence of localized scleroderma in a Negro is rare. The prognosis, with the use of several types of treatment in morphea and guttate morphea, is no different from untreated cases. Certain surgical procedures are of benefit in linear scleroderma. Generalized systemic scleroderma (including acrosclerosis) is reported following the onset of any type of localized scleroderma in 6 (5.7%) out of the 106 patients followed in this series.

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ABSTRACT OF DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Linear scleroderma is the one form which usually begins in the early decades. The incidence of hemiatrophy and the proportion of cases which manifest spinal abnormalities, often of the occult type, are significant. Calcinosis occurs occasionally in linear scleroderma but not nearly so often as in acrosclerosis.

The status of guttate morphea is tenuous. We are seeing few patients now whom we are willing to classify in this category. It is likely that many of the earlier patients in this group were affected with lichen sclerosus et atrophicus.

The authors emphasize the development of generalized scleroderma in six patients who were first seen with localized forms of the disease. I have seen two such instances, which were mentioned by Christianson, but, on careful survey of these records, it is apparent that the patients may have had the generalized form of the disease from the beginning. With the recent emphasis on systemic sclerosis and visceral involvement in generalized scleroderma, we have been screening our patients more carefully in the beginning. Those who seem to show rather insignificant tightening of the skin of the hands with Raynaud's phenomenon, for example, may be found to have evidence of esophageal involvement by physiologic tests, even though fluoroscopic studies with the use of barium show no gross disturbance of motor function.

The question of early scleroderma progressing into generalized scleroderma finds its counterpart in the subject of lupus erythematosus, where puzzling cases apparently in the discoid phase seem to develop into systemic lupus erythematosus. If adequate checks had been made earlier, some evidence of systemic disease might have been uncovered.

Progressive diffuse scleroderma is of serious prognostic import, and patients may die within a few months or one or two years from the onset, but, in the early stages, the involvement of the trunk or the extremities may truly simulate localized morphea. In the future, it will be well for us to pay more attention to the classification of the disease in its earlier manifestation, especially with an eye to future developments.

The authors mention a remarkable instance of therapeutic response to parathyroidectomy. Our experience with this has been nil. We have not been able to reconcile the enthusiastic claims of the early observers reported prior to 1939 with the almost complete silence on the procedure in the literature since that time. In such cases, perhaps, we have been too strict in our search for conventional evidences of parathyroid dysfunction, which are notoriously lacking. It may be that the parathyroid has other functions, still unknown. The subject will bear further investigation.

The cause of scleroderma remains obscure. I have been interested in the forms of scleroderma which appear in association with cutaneous porphyria. Usually, the exposed surfaces are predominantly affected, but not always so. One patient recently observed showed localized scleroderma of the berlocque distribution in association with porphyria cutanea tarda. It is intriguing to realize that treatment by chelation, edathamil, has been recommended in both scleroderma and porphyria with some measure of success. Perhaps, there is an etiologic clue in this direction.

I wish to call to your attention a patient who apparently has scleroderma. He has the yellowing of the skin, and you have all seen patients with porphyria cutanea tarda, who have localized forms of morphea or scleroderma on the face and on the hands; in a number of instances the condition has been generalized. The patient I mentioned with the so-called Addison's keloid is next to claim your attention.

The patches of scleroderma were seen below the left clavicle and a little on the right. There

were specks over the upper shoulders which looked almost like lichen sclerosus. This patient had melanosis and hirsutism and, on further investigation, beyond the scleroderma and the morphea, or the scleroderma which was confirmed by biopsy, we found that there was porphyria cutanea tarda present to account for the peculiar changes in the pigmentation and hirsutism. In this patient, there were none of the bullous reactions usually associated with porphyria.

DR. EARL D. OSBORNE, Buffalo: In 1920, while at the Mayo Clinic, I reported three cases of morphea associated with hemiatrophy. At that time, we became very much interested in the question of trauma. After that experience, for a good many years, we had every patient with scleroderma have a thorough neurologic examination by a neurologist.

It is interesting in how many patients abnormalities of different types of sensation were discovered by this neurologist, but not in all. I have always felt that localized scleroderma represented some form of trophoneurosis; early, especially after my experience at the Mayo Clinic, we began to question all patients very carefully regarding trauma, and, in many of the patients, we got a history of trauma either to the spine or to the skull, a history of a fall or a blow that induced unconsciousness or where the patient "saw stars." Furthermore, many of these patients had a history of rather severe virus infections of one type or another.

I bring this up because we have kept all our material, but I could never prove anything, I felt, because it is such a difficult subject. However, I would urge you to quiz your patients carefully regarding trauma 3, 6, or 12 months before the onset of the disease, or some history of severe virus infection. It may lead to more knowledge regarding damage to certain basal ganglia as the real cause of this disturbance.

DR. STURE A. M. JOHNSON, Madison, Wis.: Inasmuch as a remark was made regarding the chelating compounds in sclerodermatous conditions, I thought I might say a few words, since we have published two papers citing the use of the chelating compounds in three cases of acrosclerosis (*J. Invest. Dermat.* 29:273 [Oct.] 1957) and in one case of cutaneous porphyria with porphobilinogenuria (A. M. A. ARCH. DERMAT. 77:559 [May] 1958).

We feel that though the chelating compounds have great therapeutic promise their value may be in opening some new thought in the etiology of disease. By loading patients with L-tryptophan we find changes in urinary metabolites, which presently seem to be unique for a particular disease or group of diseases (*J. Invest. Dermat.* 29:289 [Oct.] 1957). There is much to suggest that in acrosclerosis the chelator unblocks magnesium for normal enzymatic function and in porphyria, zinc.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Many years ago, even before I came to the Clinic, in 1925, Dr. George Brown and Dr. Adson, a neurosurgeon, and Dr. Paul O'Leary treated different types of scleroderma with sympathectomies. We finally gave up that method of treatment, as the follow-up showed that it was not very satisfactory. Then, shortly before Dr. O'Leary died, he spent three days in my laboratory trying to get me to find the differences pathologically between various types of localized and generalized forms of scleroderma, including acrosclerosis. We were able to find only minor differences, as published in the paper with Ragsdale in the ARCHIVES.

Christianson, at the Clinic, reviewed cases of localized forms of scleroderma in children. In regard to scleroderma "en coup de sabre," there was a famous case many years ago, where a senior dermatologist was sued for a fabulous sum because they said that the patient had had some x-ray treatment and the area of alopecia was due to x-ray. However, histopathologically I was able to show that even though in scleroderma we do have obliterative changes in the blood vessels we do not have the other histopathologic changes of radiodermatitis.

DR. ARTHUR C. CURTIS, Ann Arbor, Mich.: In all probability, Dr. Brunsting may be right when he says that it may be possible that those patients who had disseminated sclerodermatous disease in our series were actually patients who had two diseases. They had a localized form, and they may have had the beginning of the generalized form, which was not recognized. Certainly, I have seen instances where this has occurred.

I was very glad to hear him mention, in some instances, the association of porphyria cutanea tarda and localized scleroderma.

Dr. Osborne's discussion of the relationship of trauma to scleroderma and the sensory changes which occur in these patches, particularly in linear scleroderma, has been my experience as well.

In regard to Dr. Johnson's discussion of chelating agents, I should like to refer to a study Dr. Earle Osborne did when he was at the Mayo Clinic which showed one of the early changes in scleroderma to be a deposition of calcium in the corium. That led to Dr. John Rukavina's work with edathamil sodium. At the present time, we have now treated 40 patients with edathamil sodium, and our results have been rather striking. Of the 40 patients whom we have treated, two had a fairly generalized morphea, and it was rather surprising to me to see the rapid disappearance of the morphea and the softening of the skin, even during the period of the treatment.

Another thing that was interesting in this series was one patient who came in with two gangrenous fingers. This was shown to be due to calcinosis

at the tips of the fingers, where she had big calcified tufts. She had contrived a protective shield which let in air in these gangrenous fingers, so we did not touch that at all but left it on while she was getting 45 gm. total of edathamil. By the time that she had finished the treatment, the gangrenous areas had separated and beneath each fingertip epithelization had occurred.

Clinical Notes, New Instruments and Techniques

Proteolytic Debridement of Hyperkeratoses of Palms and Soles

DATTATREYA N. MULAY, M.D., and FREDERICK URBACH, M.D., Buffalo

Concentrated solutions of urea have long been used for their proteolytic activity in organic analytic chemistry. When three patients with extremely severe hyperkeratoses of the palms and soles were seen in the dermatology outpatient department of the Roswell Park Memorial Institute, it occurred to one of us (F. U.) that the protein-splitting effect of this simple chemical could be of therapeutic usefulness.

Proteolytic debridement was carried out as follows: The palms of both hands and the soles of both feet were immersed in a 30% solution of commercial urea powder in water for periods of approximately 30 minutes. On examination immediately after urea soaking, the keratoses and cutaneous horns appeared whitish and translucent and the surfaces felt soft and slippery. As much as possible of the surface keratin was removed with a sharp scalpel, care being taken not to injure the deeper areas. The procedure was repeated twice daily until all the thickened keratin had been removed. The remaining rough spots were gently planed with a wire brush, care being taken that it did not go deep enough to cause bleeding. The course of therapy lasted approximately four to five days (Figure). The procedure was painless, and no ill effects were noted. The patients experienced marked relief from discomfort, which became evident after the first or second day of therapy.

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From the Department of Dermatology, Roswell Park Memorial Institute. Present address of Dr. Urbach: Skin and Cancer Hospital of Philadelphia, Philadelphia.

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Fig. 1.—*A*, arsenical keratoses of the soles prior to therapy. *B*, same patient, immediately after proteolytic debridement.

Onychomycosis Due to Microsporum Gypseum

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Human nail infections due to members of the genus Microsporum are not often encountered (M. audouini,[1] M. canis,[2,3] and M. gypseum[4,5]). Since to our knowledge nail infection by M. gypseum has not yet been described in the American literature, the following case report may be of interest.

A white female teacher aged 34 years was first seen on Oct. 12, 1957. She complained of nail changes which appeared six weeks prior to her first visit, involving the right ring and middle fingers and the left ring finger.

Examination revealed the following: The distal portion of the left ring fingernail showed disintegration, thinning, and scaling. The distal portions of the right ring and right middle fingernails were absent. The exposed nail beds were covered with scales. All three of these fingernails presented a grayish brown discoloration.

Microscopic examination of combined scrapings from the involved nails showed fungous mycelia, and M. gypseum was isolated in culture. The isolate was completely typical both grossly and microscopically for M. gypseum.

An ointment containing salicylic acid 3% and ammoniated mercury 5% were prescribed. The involved nails improved very rapidly, and after eight weeks of treatment there was only a slight brown discoloration on the distal edges remaining. However, microscopic examination at that time was positive for filaments, but all cultures were negative. The patient was again seen about four months later, and at that time the nails appeared completely normal and mycologic examination was entirely negative. No medication has been used for two months prior to this last visit.

Submitted for publication June 16, 1958.

From the Department of Dermatology and Syphilology (Dr. Marion B. Sulzberger, Chairman) of the New York University Post-Graduate Medical School and the Skin and Cancer Unit of University Hospital.

Summary

A case of onychomycosis due to Microsporum gypseum is described. Response to salicylic acid-ammoniated mercury ointment was relatively rapid ammoniated mercury 5% was prescribed. The and complete.

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Papulonecrotic Tuberculids of Glans Penis

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Papulonecrotic tuberculids of glans penis alone, or associated with other lesions elsewhere on the skin, have been so far reported only in a few instances.[1-16] To our knowledge, no such case has been reported from America.

When the lesions are limited only to glans penis, the diagnosis can be sometimes difficult, and other conditions occurring on the glans penis, such as atypical soft chancre, syphilis, recurrent herpes simplex, or cancer should be considered in differential diagnosis. Histological findings in these cases are not always conclusive, giving sometimes a rather unspecific (Reference 7, Cases 1 and 2; Reference 10, Case 1) or tuberculoid (Reference 11, Case 2; Reference 10) picture. Prolonged course, sometimes of many years,[7,8,10,11,14] spontaneous healing and recurrence, presence of the focus in the organism, and histological investigations, can be of help in differential diagnosis.

After the first six cases, which originated from Japan,[1-6] came Helleström's paper,[7] in which, describing two cases, he drew attention to this unusual site of papulonecrotic tuberculids. It is interesting to note that altogether from nine cases reported from Europe and found in literature available to us, seven were observed in the Scandinavian countries. From the remaining two, one was reported from Holland[12] and one, from Yugoslavia.[14]

Report of a Case

The patient, aged 33, the only child of healthy parents, presented himself to the outpatient department because of small ulcerations of glans penis of two years' duration. Ulcers usually appeared in crops, two to three at a time, and lasted two to three months. Elementary lesions which were like "deep furuncules" soon ulcerated and on healing left depressed scars. So far he has had four such flares; each time healing ensued spontaneously.

During the last war, when he was in a concentration camp, he had many small lesions on both legs. Their centers necrotized, and they left scars. The time from the appearance of the lesions to their scarring was about four months; the lesions never recurred again. Apart from this, he has always enjoyed good health.

Submitted for publication May 25, 1958.

From the Department of Dermatology and Venerology, University of Belgrade (Head, Prof. S. Ilić, M.D.).

Scars of former ulcers.

On examination there could be seen on the glans penis three small round ulcers, each the size of a lentil. They had a crater-like shape, with a floor covered with pus. Edges were level with the surface. Oval and irregular scars, the sites of former ulcers, were also present beside the fresh ones (Figure).

On the legs there was a great number of punch-out scars.

On general examination an active focus of tuberculosis could not be detected. There was no history of tuberculosis, either in the patient or in his near family.

Laboratory Findings.—The Nathan-Kallós test was after 24 hours negative; after 48 hours, erythema, and after 72 hours, strong edema, oozing, and superficial necrosis occurred.

White and red blood cell counts were normal. Erythrocyte sedimentation rate was 4/10 (after Westergren). Urinanalysis was normal. Wassermann test was negative. No acid-fast bacilli could be detected in the smears taken from the floor of the ulcers.

In the presence of papulonecrotic tuberculids of the legs, the diagnosis did not come into doubt. Histologic investigations were not thought to be indispensable, especially, as mentioned previously, as they are not always conclusive (Reference 7, Cases 1 and 2; Reference 10, Case 1). The patient was a young man, reluctant to any surgical intervention.

Treatment with streptomycin (30 gm.) and isoniazid tablets brought a steady improvement.

Ascorbic acid (vitamin C) in large doses was also given. After 40 days the ulcerations healed, leaving depressed scars. When last seen, three months later, there was no recurrence. The patient was advised to continue with isoniazid and ascorbic acid tablets, which he had been taking continuously since his discharge from the hospital.

Comment

The formation of tuberculids is explained by the hematogenous dissemination of bacilli from a focus in the organism. The bacilli are emitted into the blood in crops, producing different lesions, depending on the site of reaction and the sensitivity of the person. Papulonecrotic tuberculids belong to the hyperergic group, the reaction occurring in the dermis.

It could be expected that, since in our patient papulonecrotic tuberculids had been already present on the legs, a new dissemination-eruption should be expected on the legs. Why in our case the second eruption was manifested only by the appearance of papulonecrotic tuberculids on the glans penis, no new lesions or the recurrence of old occurring on the legs, cannot be answered. It can be speculated that there was a change in the local reactivity of tissues.

The cases in which, beside typical papulonecrotic tuberculids elsewhere on the body, ulcerations occur on the glans penis, corroborate the diagnosis of papulonecrotic tuberculids in recurrent ulcerations of long standing, when these are situated only on the penis.

46a, Nemanjina St.

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Correspondence

SYNTHETIC URINE AS A LOCAL THERAPEUTIC AGENT IN DERMATOLOGY

To the Editor: In the article on synthetic urine as a local therapeutic agent, by Thomas Butterworth (A. M. A. Arch. Dermat. 78:91 [July] 1958), the superiority of this treatment of necrotic leg ulcers has been found.

I remember having treated a patient 35 years ago, who tried her old home remedy, compresses with her own urine, to get rid of deep large leg ulcers.

The patient, a female cook in her sixties, came to my office with her employer, an old general of World War I fame, in Austria. She was suffering from extended acute oozing dermatitis of both legs up to the knees and had used urine compresses for more than a week to heal her large leg ulcers.

The patient and the general stated that urine compresses have been a well-known home remedy for chronic leg ulcers in the eastern part of Austria (now Hungary and Poland) for decades in peasant families. Before today I had not seen a similarly treated patient.

Rudolph S. Lackenbacher, M.D.
4753 Broadway
Chicago 40.

Obituaries

CLYDE LOTTRIDGE CUMMER, M.D.
1882-1958

Dr. C. L. Cummer was born at Cadillac, Mich., on Feb. 23, 1882, and died, after a long-standing hypernephroma with complications, on June 7, 1958. His father was a physician, Dr. Robert James Cummer, a Canadian by birth, and his mother was Abbie Stone Cummer.

Dr. Cummer received his early education in the public schools, graduating from Central High School in 1900. His college education was received at Adelbert College of Western Reserve University. He obtained his Ph.B. in 1904 and his M.D. at the medical school in 1907. He served on the medical service at the Lakeside Hospital.

Dr. Cummer seemed to take to teaching in medicine as almost a part of his life, and he became Associate Professor of Pathology, through which position his interest was directed to syphilis. Along with the late Dr. Richard Dexter he

CLYDE LOTTRIDGE CUMMER, M.D.
1882-1958

operated a laboratory for diagnosis and serology, which was very successful. Through this turn of events, it was natural for him to turn to dermatology and syphilology; he eventually became Assistant Clinical Professor of Dermatology and Syphilology in the Medical School. He was Visiting Dermatologist at Charity Hospital and Consultant at St. Alexis Hospital.

He did graduate work at the Vanderbilt Clinic and College of Physicians and Surgeons in New York City, from 1924 to 1925. Here he fell under the influence of Dr. John Fordyce, with whom he worked in his office. Dr. Cummer

literally worshiped this great dermatologist, and he never got tired of extolling him.

He served all the offices of the Ohio State Medical Association and organized a five-year plan for regional postgraduate lectures in medicine.

In World War I he served on the U. S. Selective Service Medical Advisory Board No. 7, in 1918, and in World War II, the Board of Appeals No. 8, 1942 to 1947; he later served on the Appeal Board, North Federal Judicial Districts 1951 to 1952.

He was active in the reorganization of the the Cleveland Academy of Medicine, of which he became Director from 1925 to 1927, inclusive. He served on innumerable committees and received "The Distinguished Service Reward" in 1947.

He was a diplomate of the Academy of Dermatology and Syphilology in 1933 and its President in 1947-1948. He was Chairman of the American Medical Association Section of Dermatology and Syphilology in 1944 and its Treasurer for years.

The work that Dr. Cummer did in his post as head of exhibits in the Academy of Dermatology and Syphilology will never be forgotten. It lasted over many years and went far toward paying all the expenses of the Academy.

A monument to him will be his part in the construction of the Allen Memorial Medical Library in which the Cleveland Academy of Medicine is also housed.

At the time of his last illness, he was still engaged in writing the life of the colorful Dr. Henry Handerson, a Northern boy who had drifted to the South, liked it there, and when the Civil War began joined the Confederacy and was eventually captured. After the war was over, he settled in Cleveland and had much influence in the fruition of our medical library, of which he was Librarian for a period. It is hoped that this labor of love will eventually be published by the medical library.

He and his wife, Marion, in later years have resided at 19101 Van Aken Blvd., Shaker Heights 22, Ohio. He leaves a son, married but with no children, who lives in Oak Park, Ill., and a daughter, Katherine C. Vail, with a husband, Lansing; they have three children.

Dr. Cummer was a member of Beta Theta Pi, Sigma Xi, Phi Beta Kappa, Nu Sigma Nu, and Alpha Omega Alpha. He was the author of the genealogic memorabilia of the Cummer family and wrote a manual of clinical laboratory methods, 1922, 1926, and 1931. Moreover, he was a frequent contributor to medical publications.

In the summertime he and Marion had for many years gone up to the Columbus Club at Indian River, Mich.

A great man has gone from our midst.

HAROLD COLE, M.D., Cleveland

Dr. Clyde Cummer's Role in the Affairs of the American Academy of Dermatology and Syphilology

Many among the original members of the organizing committee of the American Academy of Dermatology and Syphilology had known of the talented executive ability, in addition to the widespread scientific interests, of Dr. Clyde Cummer in his role in the formation and operation of the Cuyahoga County Medical Library in Cleveland and also as President of the Ohio State Medical Society. He had never had the opportunity to demonstrate his great abilities to the dermatologists of the entire country. However, at the time of the organization meeting of the American Academy of Dermatology and Syphilology in 1937, in Detroit, he was elected to a three-year term as a member of the Board of Directors. At the first meeting of the Board of Directors he was elected Treasurer of the Academy. He was a wonderful Treasurer and promptly put all of the affairs of the Academy on a business-like basis, which has made things easier for his successors and which has served as a model for other academies.

Because of his interest in the finances of the Academy as well as of its scientific achievements, he undertook at once to develop the technical and commercial exhibits with a view to increasing the income of the Academy and thus to help defray the expenses of the annual meetings. At the time of our first meeting in St. Louis, the income from exhibits was modest. At the time of his retirement as Director of Technical Exhibits, the income from the exhibits had increased tenfold.

Not only did Dr. Cummer develop the technical exhibits in quantity, but, what is far more important, he improved the quality and maintained them at the highest ethical standards. Thus we have no "advertising" cocktail parties, dinners, or entertainments, largely through the efforts of Dr. Clyde Cummer, and every member of the Academy should feel proud of it.

During the developmental years of the Academy from 1937 to 1941, and again in 1946 and 1947, it became increasingly clear to Dr. Cummer, as Treasurer, and to me, as Secretary, that the functions of these offices should be combined in the interests of efficiency and economy. These offices were combined in 1947 and assigned to a younger man. Dr. Cummer retained the position and title of Director of Technical Exhibits. In 1948, Dr. Cummer was honored by election to President of the American Academy of Dermatology and Syphilology. At the request of the Board of Directors, he retained his position as Director of Technical Exhibits and continued to do so until 1957, when a successor whom he had chosen took over.

Dr. Cummer was always intensely interested in the scientific exhibits. For many years he served on the committee which judged these exhibits. His judgment was greatly respected by all other members who served on this committee. Also, it was largely through his efforts that certain sums of money were contributed by friends for the advancement of the scientific exhibits.

Certainly, all members of the American Academy of Dermatology and Syphilology owe a great deal to the memory of Dr. Cummer for the part which he played in its organization and functioning and for the extensive time and effort which he put into its many endeavors. We need more men like Dr. Clyde Cummer in our specialty.

EARL D. OSBORNE, M.D.
Buffalo.

LLOYD WARREN KETRON, M.D.
1885-1958

Dr. Lloyd Warren Ketron was born in Bloomingdale, Tenn., on May 21, 1885. He was graduated from the U. S. Grant University of Chattanooga, Tenn., in 1907, and received his M.D. degree from The Johns Hopkins University in 1911. From 1911 to 1912 he was a special student in dermatology under Dr. T. Caspar Gilchrist, the Clinical Professor of Dermatology. After his training under Dr. Gilchrist, he spent a year in the dermatology clinics of Austria and Germany, studying under the great masters of dermatology. During his year in Europe he became interested in the pathology of the skin. When he returned to Baltimore, in 1912, he established an office and was appointed Assistant Dermatologist in the outpatient department of The Johns Hopkins Hospital. He was promoted to Attending Dermatologist in 1917. From 1913 to 1917 he was

LLOYD WARREN KETRON, M.D.
1885-1958

an Instructor in Dermatology. From 1917 to 1924 he was an Associate Professor of Dermatology and Head of the Division of Dermatology in the Department of Medicine. During his long association with The Johns Hopkins Hospital he made many important contributions, especially in the field of dermatohistopathology. In 1928 Dr. Ketron established the laboratory of dermatohistopathology. At about the same time he reorganized the Dermatology Clinic and equipped it with modern facilities. Dr. Ketron was a popular teacher, and the medical students always attended his lectures with great enthusiasm. His particular interest, how-

ever, was in his laboratory. Over the years Ketron's Laboratory became a famous center for dermatohistopathology, and dermatologists throughout the United States referred their problem cases to him for his expert opinion. The collection of skin biopsy specimens in Ketron's Laboratory is one of the largest in the United States and will be of invaluable benefit to future students of dermatology. After Dr. Ketron's formal retirement, in 1956, he continued to work in his laboratory. Even during his terminal illness he constantly asked about the activities of the laboratory, and he was concerned about the biopsy reports.

Dr. Ketron was a Founder member of the American Board of Dermatology and Syphilology. He was a member of the American Dermatological Association, the American Medical Association, the American Academy of Dermatology and Syphilology, the Society for Investigative Dermatology, the Baltimore City Medical Society, and the Southern Medical Association. He was a member of The Johns Hopkins Faculty Club, and the Caduceus Club. He was a former member of the Elkridge Club, the Baltimore Country Club, and the Gibson Island Club. Dr. Ketron has been a familiar figure in the doctors' dining room of The Johns Hopkins Hospital for many years. Although he held memberships in the clubs listed above, actually his real club was the doctors' dining room, where he loved to meet with his associates and exchange pleasantries in a relaxed fashion which characterized his personality. His hobby was fishing. His family life was very attractive. He loved his children and his grandchildren. Entertainment by the Ketrons usually centered around their family and their activities at home. Many of his friends who had the opportunity of being entertained in his attractive home on St. Paul St. recall happy hours of informal good times.

He is survived by his widow, Romola Cressey Ketron; his daughters, Mrs. Barton Harrison and Mrs. R. Emmet Bracken, and five grandchildren.

We all mourn the passing of this fine man who was a distinguished physician, a first-rate investigator, and a true friend.

In 1956, the Division of Dermatology of The Johns Hopkins Hospital established an annual lectureship which is known as the Lloyd W. Ketron Lecture. Thus far, two distinguished dermatologists have presented Ketron Lectures. It is hoped that, through this medium, Dr. Ketron's name will be kept alive and that the Ketron Lecture will bring to The Johns Hopkins Hospital in future years many distinguished dermatologists to honor his memory.

MAURICE SULLIVAN, M.D.

JESUS GONZALEZ URUENA, M.D.

1868-1957

We have learned of the death of Dr. Jesús González Urueña, in México, D. F., on Sept. 29, 1957. He was a Corresponding Member of the American Dermatological Association. During his long life (1868-1957), he aided greatly in the improvement of dermatology in his country. He was Professor of Dermatology of the School of Medicine of the National University and the outstanding teacher of dermatology until his retirement, in 1928. Thanks to him, interest in syphilis was revived, the systematic study of the mycoses was initiated, and cutaneous tuberculosis was recognized as a health problem. His knowledge of leprosy is reflected in his book, "La lepra en Mexico" (1941).

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Morris Leider, M.D., President

Henry Silver, M.D., Secretary

Feb. 13, 1958

Recurrent Hemorrhagic Purpura of the Legs with Ulcer Formation. Presented by Dr. Max Wolf.

Ten months ago, reddish spots appeared on both lower extremities of a 27-year-old woman three weeks after a severe sore throat. They were accompanied by swelling of the ankles and severe pain in both knee joints. In the following month the reddish puncta enlarged, their color darkened, and their centers became vesicular, crusted, and finally ulcerated. It took five months for the ulcerations to heal. During this time the patient attended medical, dermatologic, and arthritic clinics. She was discharged with the diagnosis of "rheumatoid arthritis" and was advised to continue to take aspirin, which she did, in amounts of 10 to 12 tablets daily. Four months ago, the patient complained again of sore throat and earache. Three weeks later the second attack of her skin disorder started with reddish spots first on one leg, later on the other. In the ensuing two months the number and size of the lesions increased and some became extremely painful. The patient was unable to walk, and the legs were considerably swollen.

Upon first examination no edema or varicose veins were seen on the legs. A good peripheral pulse was palpable. On the dorsa of the toes, the insteps, and the sides of the feet there were a few pinpoint- to millet-seed-sized hemorrhagic spots. On the inner and outer aspects of both lower legs there were numerous, discrete, round, oval, or irregularly shaped 5 mm. to 1 cm. dark hemorrhagic lesions. Many of the lesions showed a necrotic center and were surrounded by an erythematous halo (Fig. 1).

Later the larger lesions around the right inner and right outer ankle ulcerated. In the center of the medial aspects of the legs the lesions crusted heavily. Most of the remaining lesions healed with pigmentation.

Biopsy specimen taken from a hemorrhagic lesion did not reveal any distinctive changes.

Submitted for publication April 9, 1958.

An otolaryngological examination did not reveal any pathologic findings except slight enlargement of the tonsils. A smear from the tonsils was negative.

Extensive laboratory studies including, aside from routine procedures, bleeding and coagulation times, creatinine levels, cryoglobulin and electrophoretic protein determinations, search for L. E. cells, blood culture, and study of bone marrow pattern yielded essentially normal findings. The antistreptolysin titer was 333 units.

Discussion

Dr. Frances Pascher: My impression is that we are dealing with necrotizing vasculitis attributable to a streptococcal infection. Both episodes of hemorrhages into the skin with subsequent ulceration were preceded by a sore throat with fever. This hypothesis is supported by the increased antistreptolysin titer. The ingestion of salicylates over a prolonged period may also be significant. The drug per se or in combination with the bacterial agent (haptene) may sensitize the vessels and thus induce a vasculitis. Another possibility to be considered is depletion of vitamin C by salicylates. This can be established or excluded by means of the Harris and Ray vitamin C saturation test.

Dr. Nathan Sobel: Following scarlet fever, I have seen crops of inflammatory nodules which rapidly develop into ecthymatous lesions. The Shwartzman phenomenon suggests itself in consideration of pathogenesis of such events and may also be applicable in this instance.

Dr. Conrad Stritzler: Antistreptolysin titers, unless very high, ranging around 1200, or rising steadily from a previous low point, must be interpreted with caution. I would consider a titer of 300 insignificant, or of doubtful significance.

Dr. John Garb: By investigating the cryoglobulins, Dr. Wolf revealed his awareness of the importance of such tests in patients with purpuric eruptions and ulcerations of the lower extremities. The presence of cryoglobulinemia is more likely when similar lesions are associated with hepatomegaly with or without splenomegaly.

Fig. 1.—Clinical aspect of recurrent hemorrhagic purpura with ulcer formation.

DR. MAX WOLF: The mechanism of the origin of this recurrent purpura with ulcer formation is rather obscure. The unusual clinical features resemble closely the picture of the Sanarelli-Shwartzman phenomenon (Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940). Slepyan observed during World War II, in a great number of hospitalized soldiers, purpuric eruptions of the lower extremities. It was found that these soldiers had had an infection of the upper respiratory tract 1 week or 10 days prior to the appearance of the purpura (Slepyan, A. H.: *A. M. A. Arch. Dermat. & Syph.* 63:646, 1951). A variety of syndromes whose common denominator is an allergic vasculitis (Szymanski, F. J.: A. M. A. ARCH. DERMAT. 75:288, 1957) may occasionally show purpuric eruptions with necrosis and ulcer formation. Cutaneous manifestations of polyarteritis nodosa (Lyell, A., and Church, R.: *Brit. J. Dermat.* 66: 335-343, 1954), nodular dermal "allergides" of Gougerot (Gougerot, A., and Duperrat, B.: *Brit. J. Dermat.* 66:283-286, 1954), allergic cutaneous arteriolitis (Ruiter, M.: *Brit. J. Dermat.* 66:174-181, 1954), hypersensitivity angiitis (Zeek, P. M.: Am. J. Clin. Path. 22:777, 1952) may be regarded as different designations for a similar group of diseases of more severe character where a necrotizing vasculitis may be found as an underlying pathology. The fact that in our case the microscopic picture did not reveal changes of the blood vessels corresponding to the clinical features does not speak against the allergic pathogenesis. The biopsies were performed six weeks

after the onset of the purpura, at a time when the eruption was in a subsiding stage.

Lichen Nitidus with Nail Changes. Presented by Dr. A. J. ORFUSS and DR. S. KATZ (by invitation).

A 21-year-old woman noticed an eruption on the wrists six months ago. This condition has progressed slowly and has not been accompanied by subjective symptoms. About one month ago nail changes appeared.

On examination, the patient shows pinhead-sized, slightly raised, discrete, yellow-brown papules on the flexor aspects of the wrists, in the cubital fossae and axillary folds, and on the right vulvar lip. Some fingernails show pitting, principally in the region of the lunula.

Histologic examination was reported by Dr. A. Hyman as follows: "The epidermis shows areas of suprapapillary thinning and here the basal margin is washed out. The papillae are occupied by fibroblastic lymphocytes, a few cells of epitheloid type, and edema. Although the aggregates are not quite diagnostic, they are confirmative of the lichen nitidus nature of the lesions."

Discussion

DR. NATHAN SOBEL: The patient has typical lichen planus of the buccal mucosa. Lichen planus of the nails occurs rarely. I have seen stippling of the fingernails in a patient who had lichen planus and believe the presented case shows nail changes due to lichen planus. V. Pardo-Costello (Diseases of the Nails, Springfield, Ill., Charles C Thomas, Publisher, 1946) states that when lichen planus affects the nails longitudinal striations occur more often. Also noted is the occurrence of transverse lines and, rarely, punctiform depressions in the nails like those of psoriasis.

DR. MAX WOLF: In many cases of generalized lichen planus I found different changes of the nails as longitudinal ridges, distortions, and channel formations of the nail plate. These changes may not be regarded as pathognomic but rather as an expression of atropic disturbances (Arzt, L., and Zieler, K.: Die Haut und Geschlechtskrankheiten, 1935, Vol. 2, p. 455).

DR. A. J. ORFUSS: I must say that when I first examined this patient I was not impressed with the nail changes as being other than the usual pitting which occurs following an eczematization in the region of the matrix. I do not believe that these changes are characteristic of lichen planus.

DR. CONRAD STRITZLER: I should like to enter a dissenting opinion. I believe these nail changes are most compatible with psoriasis, appearing coincidentally in a patient with lichen nitidus.

Sarcoidosis; Improvement Following Therapy with Iproniazid (Marsalid). Presented by DR. CONRAD STRITZLER.

A Negro man, aged 41, born in Georgia, is presented with a history of several years' duration of repeated episodes of cough, expectoration of thick yellow sputum (never blood-streaked), and a papular eruption on the face, arms, and legs. During the past two years he has been hospitalized on two occasions for two to three weeks because of fever, weakness, cough, and expectoration and has been discharged with the diagnosis of "pneumonitis." He had a penile lesion in 1943, for which he received "rapid treatment" at Bellevue.

Examination one year ago showed a nodular eruption about the eyebrows, especially about a scar over the left eyebrow, and on the arms, forearms, and legs. They were bead to hazel nut in size, smooth, skin-colored, and not tender. Nothing distinctive was seen on diascopy. There was enlargement of lymph nodes in the anterior cervical triangle, left supraclavicular region, axillae, and groins. The heart was somewhat enlarged to percussion, but otherwise negative. A blunt liver edge was palpable 3 fingerbreadths below the right costal margin, and the splenic edge was definitely palpable on deep inspiration. The fingernails showed clubbing.

The VDRL and T. P. I. tests were positive. X-ray examination of the chest showed marked enlargement of the hili with disseminated infiltration throughout both lung fields which was read as sarcoidosis. Reexamination one month later showed no change. Nine months ago iproniazid was prescribed (50 mg. t. i. d.). Six weeks later, x-ray examination of the chest showed marked resolution compared with previous plates. About one month ago, after iproniazid therapy had been discontinued for four months, x-ray examination of the chest showed considerable enlargement of the hilar shadows, and oval density at the right superior mediastinum suggestive of adenopathy, and an enlarged heart. X-ray examination of the hands and feet showed no evidence of osseous pathology.

Tuberculin tests were negative repeatedly. A Kveim test became positive in three months and still persists. Culture of sputum for tubercle bacilli was negative. Total proteins were 8.3 gm., with albumin 3.9 gm., globulin 4.4 gm. Biopsy specimen of a nodule from the left eyebrow showed the dermis to be infiltrated with small tubercle-like granulomata consisting of epithelioid cells, giant cells, and lymphocytes, without caseation. The histological diagnosis is sarcoidosis.

Discussion

DR. MORRIS LEIDER: Iproniazid is an antituberculous drug—although less effective than

isoniazid. If this is truly a case of sarcoidosis and if the iproniazid therapy is truly the cause of improvement, then this is an argument of some weight that some cases of sarcoidosis are of tuberculous origin.

DR. FRANCES PASCHER: I do not want to be in the position of detracting from the apparent excellent therapeutic result obtained in this case. It is notoriously difficult to evaluate therapy in sarcoidosis because of its variable course. Edelson, (*J. Invest. Dermat.* 21:1-3, 1953) has reported favorably upon iproniazid in tuberculosis, whereas H. L. Israel, et al. (*Am. Rev. Tuberc.* 67:671-673, 1953) found iproniazid ineffective. A more extensive trial with this agent in sarcoidosis is warranted, particularly in view of the low incidence of untoward side-effects.

DR. CONRAD STRITZLER: No claim is made that iproniazid caused the remission in this patient. However, the rather prompt improvement in the cutaneous and pulmonary manifestations following the institution of iproniazid therapy is interesting. Three of seven patients with sarcoidosis currently under observation show similar improvement.

The pulmonary lesions cleared strikingly and relapsed after the discontinuation of therapy. The cutaneous lesions have remained clear now for several months after therapy has been discontinued. We realize that this may represent a spontaneous remission. We will continue to observe these patients and will try to determine if there is a sure relation between iproniazid therapy and improvement.

I have asked Dr. Louis Siltzbach to give a number of patients with sarcoidosis iproniazid therapy, and I expect to have a report from him in a few months.

Secondary Syphilis. Presented by DR. HANS H. BIBERSTEIN and DR. C. GAY (by invitation).

A 34-year-old white man was first seen six months ago with a bright red, sharply circumscribed plaque that measured 4×6 cm. on the left malar prominence and a penny-sized erythematous plaque on the left cheek. No apple-jelly nodules were seen in any of the lesions. All the lesions were of one month's duration previous to this visit. At that time the diagnoses that were considered were lupus erythematosus, lupus vulgaris, and lymphocytic infiltration. A punch biopsy from the left cheek was reported as follows: "The upper cutis is edematous. Considerable telangiectasis is present. A massive infiltration is present in the deeper layer of the cutis. This consists of tubercles composed of giant and epithelioid cells with some mixture of round cells and lymphocytes. An occasional plasma cell is present. Diagnosis: Tuberculoderm."

Tuberculin tests were negative. Therapy was started with isoniazid (50 mg. t. i. d.). When no improvement was noticed in two weeks, isoniazid therapy was stopped. Treatment with Aralen (250 mg. b. i. d.) was started and continued for six weeks. The condition did not improve.

Serologic and treponemal tests for syphilis were then done and were found to be strongly positive. Careful reexamination of the patient revealed a macular eruption over the back. A white scar was found on the glans. The patient denied a penile sore, adenopathy, or other signs and symptoms suggestive of syphilis.

Treatment with penicillin to a total of 7,200,000 units was given in three days. Shortly after, the lesions resolved.

In view of serological findings, review of the slides was done by Drs. Sims and Pensky and was reported as follows: "On histopathologic grounds alone, it is not possible to make a diagnosis of syphilis. The presence of tuberculoid structure is found at times in syphilis (secondary or early tertiary).

Discussion

DR. IRVING D. EHRENFELD: So far in the discussion, no one has said anything about the nature of the lesions this man presented. They certainly were not examples of the ordinary secondary eruption so far as their number, appearance, or distribution is concerned. If they were syphilitic I should consider them as late secondary or precocious tertiary lesions. There may still be some question as to whether they were syphilitic in origin, even though the serologic and other tests for syphilis were positive. No mention is made in the presentation of titers and whether the titers rose or fell.

DR. NATHAN SOBEL: When the patient was seen by me four days after he received the first penicillin, the skin lesions were gone. This rapid therapeutic result confirms the serologic findings. He undoubtedly had a late type of secondary syphilis. Since the histopathologic picture could be that of late syphilis, the diagnosis of precocious tertiarism is acceptable.

DR. A. J. ORFUSS: I agree with the previous speakers, that we must think of syphilis much oftener than we have been accustomed to doing recently. I must admit that I was mislead by the definite biopsy report of a tuberculoderm. However, because of the rapidity with which the lesions vanished with penicillin therapy I am convinced that we were dealing with a form of syphilis.

Lupus Erythematosus Disseminatus with Cryoglobulinemia. Presented by DR. JOHN GARB.

A man 46 years of age presents an eruption on the face, shoulders, back, and extremities of four

Fig. 2.—Grayish-black plaque on the ear in a case of lupus erythematosus.

months' duration. As a construction worker he has been exposed for many years to the vicissitudes of weather. Lesions appeared first on the nose and subsequently on the ears, lower extremities, shoulders, and back. The patient now presents symmetric lesions on the aforementioned areas. The lesions vary from grayish-black solid plaques on the ears (Fig. 2) to slate-gray patches on the upper lip, chin, nose, and sides of the face that resemble argyria. There is no history of intake or application of silver salts. On the sides of the upper part of the neck are ill-defined, slightly raised, erythematous patches; similar lesions are present on the forearms and lower two-thirds of the arms, in which places they are covered with dry, adherent scales.

Routine laboratory tests, including determination of A/G ratio and sedimentation rate, are normal. The blood was negative for L. E. cells and rosettes. Blood serum gave a strong positive reaction for cryoglobulin. Histologic sections from the right ear lobe and from the extensor surface of the right arm were diagnosed as compatible with chronic discoid lupus erythematosus and subacute lupus erythematosus, respectively.

The patient is being treated with Aralen by mouth (250 mg. twice a day) and with a lotion containing *p*-aminobenzoic acid topically.

Discussion

DR. FRANCES PASCHER: The demonstration of cryoglobulin in this case is of considerable interest.

A test was made because of the prominent involvement of the tip of the nose and ears and the dusky complexion, features which suggest pernio or chilblains. The latter has been shown to be one of the symptoms associated with cryoglobulinemia. Moreover, the qualitative test in this case indicates that these abnormal proteins are present in considerable quantity. Another sample of serum has been sent to the laboratory for a quantitative estimate. Cryoglobulin has been noted before in association with lupus erythematosus, but it has been regarded as a relatively infrequent finding (Feldaker et al.: A. M. A. ARCH. DERMAT. 73:325-335, 1956). I think it would be of interest to test for these abnormal proteins in this disease, particularly in the presence of purpura or Raynaud's phenomenon.

Classification of this case presents considerable difficulty. Laboratory tests did not disclose any evidence of systemic involvement (unless the presence of cryoglobulin is so interpreted). On the other hand, the lesions are not localized but have spread to involve the neck, arms, and chest. Some of the lesions, furthermore, are not discoid but are ill defined, erythematous, and edematous. A biopsy specimen from such a lesion on the arm was interpreted as showing changes consistent with *subacute* lupus erythematosus, i. e., absence of plugging, and marked edema of the upper cutis.

DR. VICTOR H. WITTEN: Rather than using the name *disseminated* chronic discoid lupus erythematosus for those cases of chronic discoid lupus erythematosus presenting numerous scattered lesions over the surface of the body, I strongly favor the terms *widespread* or *generalized* rather than disseminated. Through common usage among dermatologists and internists, the term *disseminated* has become regularly associated with the subacute and acute varieties of lupus erythematosus and carries with it the implication of systemic as well as cutaneous involvement. To use the term *disseminated* to describe a case of chronic discoid lupus erythematosus with widespread involvement of the cutaneous surface will only serve to confuse. There is difficulty enough, already, with the classification of types of lupus erythematosus without adding to the confusion.

Case for Diagnosis: Epidermolysis Bullosa, Dystrophic Type. Presented by DR. CONRAD STRITZLER

A 24-year-old Negro man is presented with a widespread bullous eruption of the face, mouth, neck, axillae, hands, feet, elbows, and knees. There is no family history of this condition. It began at 13 years of age and has been continuous since, with partial remissions at times. The bullae appear upon the slightest trauma, but they may appear apparently without cause. Their content is clear to cloudy. They vary in size from that of a fingernail to several centimeters in diameter, arise on a noninflammatory base, and tend to heal with depigmentation. There is no itching.

Over the elbows and knees there are thickened and scaly areas, marking the site of healed bullae. The nails are almost entirely destroyed, leaving scarred, tapering, atrophic fingertips. Bullae are almost constantly present in the mouth. They break easily, leaving denuded areas on the surfaces of the tongue, palate, and buccal and labial mucosa.

In the laboratory work-up, the important findings are absence of abnormal porphyrins, absence of sickling, and a subepidermal bulla in the histologic section.

Treatment has consisted chiefly of administration of iron, steroids, and tetracyclines. It is doubtful that any remission has been induced by such therapy; it is probable that any change in the clinical situation has been spontaneous. However, rupial crusting and secondary infection appear if the tetracycline (in doses of 250 mg. daily) is discontinued.

Although we are unable to trace any hereditary factor in this patient, we still feel it is hereditary in origin, as a recessive trait.

Discussion

DR. HELEN O. CURTH: I object to the wording of the last sentence of the protocol, which reads: "Although we are unable to trace any hereditary factor in this patient, we still feel it is hereditary in origin, as a recessive trait." It is, however, characteristic of recessive inheritance that the disorder is not evident in the heterozygous state of each parent of the patient. Consanguinity of the parents would make recessive inheritance more probable, but it did not take place in this family. It should also be mentioned that the patient had an unaffected sister, who died at the age of 5 years. The patient was older than that when he showed the first signs of the disease, and the sister might have shown signs of the disease had she lived longer.

With regard to epidermolysis bullosa the severe form is usually inherited recessively and the mild form dominantly, as has been observed in other inherited disorders which occur in severe and mild forms. The following theory explains the difference. A patient with a dominantly inherited disease still has a normal allele (an alternative gene) which may counteract the effect of the abnormal dominant gene, whereas in the patient with a recessively inherited disease both alleles are abnormal. There are, by the way, exceptions to the rule that the milder form of a disease is inherited as a dominant and the severe form as a recessive. I recall a pedigree (MacKenna, R. M. B.: *Brit.*

J. Dermat. 49:448, 1937) in which the dystrophic form of epidermolysis bullosa was inherited as a dominant.

Preliminary Report: Comments of the Value of Phosphorus 32 as an in Vivo Method for the Diagnosis of Malignant Melanoma. By DRS. EARLE W. BRAUER, ALFRED W. KOPF and VICTOR H. WITTEN and DRS. VERNAL CAVE and MONES BERMAN (by invitation).

Diagnosis: Pigmented Nevi (Junction Type) on Eyelids of a Child. Presented by DR. LOUIS WEXLER.

LOS ANGELES DERMATOLOGICAL SOCIETY

S. W. Becker, M.D., President

Floralou Kettenbach, M.D., Secretary

Feb. 12, 1958

Lymphoblastoma Localized on the Scalp for Thirty Years. Presented by DR. MAXIMILIAN E. OBERMAYER and DR. IAN MACDONALD (by invitation).

A man, aged 56, was presented before this Society on June 13, 1944 (*Arch. Dermat. & Syph.* 53:64, 1946). Prior to that he had been studied by Dr. George C. Andrews, at the Vanderbilt Clinic, New York, in 1933-1934. In 1944 the presenter's diagnosis was that of lymphoblastoma of the leukemic or pseudoleukemic type, rather than true mycosis fungoides.

The patient was referred to Dr. Ian Macdonald for x-ray treatment. From 1944 to the present time the indurated plaques on his scalp responded promptly to the treatment but always recurred. The total dose administered during these 13 years was 25,200 r at 130 or 160 kv. and a half-value layer of 0.16 mm. Cu. The last series of treatment in 1957 was given at a H. V. L. of 0.23 mm. Cu. Therapy has been administered to 200 ports with overlapping of areas. The intervals between treatments varied from a few months to more than one year and were shorter during the past two years.

The present recurrence came on within 42 days after the last treatment.

The average dose necessary to make the lesions disappear was 200 r.

It is felt that continued irradiation is no longer a safe procedure.

Periodic blood cell counts were normal, and sedimentation rate has never been elevated. X-ray studies of the chest in 1948, 1952, 1954, and 1957 have not demonstrated any notable changes; apparent localized pleural fibrosis was seen in 1957.

Occasional general physical examinations have not demonstrated any lymphadenopathy of accessible areas or enlargement of liver or spleen.

Discussion

DR. WALTER R. NICKEL: I would like to begin the discussion of this case by recalling Dr. Lawrence Nelson's case that we all saw in Santa Barbara about eight or nine years ago. His patient also had nodular lesions on his scalp. They were of long duration, as I recall, about 15 years. Next, I'd like you to recall a woman that I presented in San Diego at least on two occasions to this group, who had a lesion which had been diagnosed here in Los Angeles clinically as sarcoid, and, when it was finally biopsied in San Diego, proved to be a lymphoblastomatous lesion. She went on for 15 years and finally died of her lymphoblastoma because it spread to the viscera after 15 years, but it remained localized for about 13 of the 15 years. Some of you may recall this woman. She liked to have these nodules "drained," and "draining" consisted of performing a biopsy after which the mass would tend to disappear. I feel certain that this is a relatively benign form of lymphoblastoma, tumorous variety, nodular type. Microscopically, I don't think there is much that you can consider except reticulum-cell sarcoma, since the number of reticular fibers was increased markedly, particularly surrounding the mass of cells. The microscopic section from biopsy in 1944 is presented; the histopathologic features are described in the printed report from the *Archives* at that time. The microscopic section from the recent biopsy is also presented and shows essentially the same features except that the band of normal collagen is broader.

DR. A. FLETCHER HALL: I would like to ask Dr. Macdonald to translate the half-value layer of copper into its approximate equivalent in aluminum so that we dermatologists, who habitually think in terms of aluminum filters, can visualize the quality of radiation that has been used on these lesions. It is very difficult for me to see any evidence of x-ray damage to the skin, but that does not rule out damage to the subcutaneous tissues, periosteum, or bone. I think very "hard" ray must have been used because of the absence of evidence of x-ray injury to the surface. I feel that more superficial x-rays could be used if needed, and that the "if needed" should depend upon what these lesions do without x-ray: If they threaten to become fungating lesions, I think there should be no reason to withhold further x-ray, particularly

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if the lesions continue to be radiosensitive as they appear to have been. Any dosage in the realm of 200 r is a relatively small dose, and I can't see why it couldn't be used repeatedly in the future if fungating lesions become threatening.

DR. LOUIS H. WINER: My diagnosis on this case, histologically, was lymphosarcoma of the reticulum-cell type because of the great number of mitotic figures and the large size of the cells seen in the histologic section. I have studied two similar cases in the past six years. Clinically and histologically they were reticulum-cell sarcoma. The diagnoses were confirmed independently by two general pathologists. Both patients had dramatic beneficial responses with complete resolution of the lesions and no recurrences following small doses of roentgen rays. I think that lymphosarcoma of the scalp is an entity in which the prognosis is better than lymphosarcoma secondary to Hodgkin's disease or that of mycosis fungoides.

DR. SAMUEL AYRES JR.: In view of the apparently benign nature of the lesion, I am wondering whether there would be any virtue to giving a trial of freezing with liquid nitrogen.

DR. S. WILLIAM BECKER: If it becomes necessary to discontinue roentgen therapy, there are other methods to benefit this patient—with no more cutaneous lesions than he has—namely steroid therapy, which is rather innocuous, and has aided in some of these tumors. The electron breeze (I think there is one available at Stanford in San Francisco) certainly has done wonders in some patients after they have received the maximum roentgen therapy. Then, of course, later, if necessary, the nitrogen mustards and similar substances could be used. I don't think you ever cure one of these patients.

DR. SAMUEL AYRES III: In view of their localized nature, I would suggest injecting hydrocortisone into the lesions. This seems worth trying because the corticosteroids, given systemically, do have a palliative effect on the various lymphoblastomas.

DR. IAN MACDONALD: The half-value layer equivalent of 0.16 mm. Cu—I would have to refer to tables for accuracy—I would say is the same as five times as much aluminum. The hazards that this man faces are not in the nature of future damage to the periosteum or bone, or the possibility of a sarcomatous degeneration, but are more analagous to the damage suffered by dentists and the old radiologists before they became aware of the dangers of minute, almost daily, doses of exposure, particularly to the skin of the hands, that you have all seen. This man is now nearly 60. He comes of a long-lived ancestry. Unless his disease becomes generalized, he may well go along until his mid-seventies. So, this danger of the development of a squamous carcinoma of the scalp is not an imaginary hazard. Recognizing the fact that more roentgen therapy is needed, I would be willing to proceed with roentgen therapy if the quality indicated—of the half-value layer that we showed. He did have a trial with prednisone (Meticorten), 25 mg. twice a day for a period of three weeks. None of the lesions showed the slightest regression. It may be that some other corticosteroid might be more effective—I don't know. I don't think that alkylating agents are indicated right now in the absence of any demonstrable systemic disease. There are hazards, and I don't think that they are justifiable when you are still dealing with a strictly localized disease. I have seen, over the years, four other patients who had long-continued localization of reticulum-cell lymphosarcoma of the scalp. One of these patients was under my observation for seven years and then escaped from follow-up. In New York from 1935 to 1938, I was responsible in part for the care of one patient who was in his 11th year of lymphosarcoma localized to the scalp—and I don't know what has happened to him since. This particular patient represents the longest duration of a strictly localized involvement of the scalp in my experience. Now the thing that intrigues me about this problem—is it a cutaneous equivalent of a localized, regional reticulum-cell lymphosarcoma in lymph node involvement? This is the form of lymphosarcoma which offers the brightest outlook in persons who have, as far as one can determine, localized disease of limited extent. The neoplasm is so favorable in cases like this that it may be another 10 years before he develops mediastinal node involvement, hepatomegaly, splenomegaly, or blood signs of bone marrow involvement. These unusual forms are analagous to the so-called desmoid tumors, which are extremely low-grade fibrosarcomas, nonmetastasizing-type, usually in the abdominal wall. They are strictly a problem in local therapeutic elimination, though they do have a tendency to recur even when the field of surgical excision has been wide. Another comparable neoplasm is Bowen's disease, which I think most of you gentlemen accept as being entirely different than ordinary squamous carcinomas of the skin. Finally, there are lesions of peripheral nerve trunks, a very few of which will exhibit multicentric areas of involvement, as many as four or more over a period of years. I am somewhat confused over this process being identified with mycosis fungoides. To me, they are separate and distinct entities. I have thought always that mycosis fungoides was a polymorphous process, whereas reticulum-cell lymphosarcoma is a disease exhibiting a monotonous histologic architecture. I should be delighted to be put straight on this point.

DR. J. WALTER WILSON: Since none of the lesions which have been present over the scalp of this patient have been more than 7 mm. in thickness, I wonder why radiation of this degree of hardness was selected. Much less penetrating forms of radiation, such as that from the betatron, cathode-ray source, or even P^{32} have been shown to be efficient in lymphoblastomas including mycosis fungoides in the tumor stage. In view of the facts that radiation is thought to cause leukemia and that some cases of lymphoblastoma, notably mycosis fungoides, can be present for years in a mild form and become lethal later, how are we to combat the impression that the radiation commonly administered during the interim was responsible for the worsening?

DR. IAN MACDONALD: This quality of radiation was deliberately selected at the onset, in contemplation of a long period of years during which many therapeutic exposures would be necessary. The H. V. L., incidentally, has been 0.16 to 0.23 mm. Cu. A patient treated by P^{32} or the so-called electronic beam or the most caustic x-radiation would have vascular damage. That is the critical issue in question. He would now have vascular damage, stromal sclerosis, and hypoxia and would present very obvious signs of radiation damage. The damage alleged to produce leukemia in radiologists is not the therapeutic exposure to which this man has been subjected. I don't think we have to worry about his genetic problem. Radiologists all wear a roentgen badge. I suggest you look at the current issue of the *J. A. M. A.* which contains an article contending that there is no significant difference in the death rate from leukemia among radiologists, as compared with other physicians, after correction for age.

DR. RALPH LUIKART II: Particularly in view of the fact that we are honored by having Dr. Macdonald, who is an authority on radiation, here with us this evening, it would seem most worth while to pause and give the problem of radiation treatment in this unusual patient some serious consideration. It sometimes appears that radiologists present a somewhat different point of view than we are accustomed to using ourselves. I am sure we are all in agreement that the total effects of radiation are solely produced by primary and secondary ionization resulting from the displacement and scattering of electrons in the tissues when struck by the electromagnetic waves. It is clear that when an electromagnetic wave does not strike an electron or nucleus in the tissue it does not produce ionization. Of those that do strike, the softer radiation results in secondary ionization, producing effects forward, laterally, and even back scattering, thereby having the majority of its ionizing effects in the upper layers of the tissues. The harder beam results in a more forward scattering of the "struck billiard balls," throwing the ionizing effect more deeply into the tissues. Hence, when a very hard beam is used the majority of the effect is at a greater depth. When the radiologist is aiming at the pituitary or ovary, it is apparent that multiple ports of delivery as well as harder beams to produce a greater degree of ionization at a depth are desirable. Now, in this particular problem the pathology lies close to the epidermis. Therefore, I believe that inasmuch as the epidermis has been so clearly spared with the huge doses of radiation that have been used, by the same line of reasoning, so has the tumor.

DR. IAN MACDONALD: The air dose translated in terms of skin dosage—again only by recall, H. V. L. 1 mm. Al, becomes anywhere from 130% to 150%. The air dose of 100 r heavily filtered produces a skin dose perhaps of only 104 r. So the major portion of the dose in terms of skin roentgens is going into the tumor—the essential difference is that of greater penetration.

DR. JACK W. GRIFFIN: The time dosages for many of our superficial x-ray machines are calibrated to include back scatter, factors for which are from Quimby et al. (1952) and *British Journal of Radiology* (Supplement, 1953).

DR. IAN MACDONALD: Our machine is calibrated in air. Skin dose has to be calculated in terms of back scatter related to square area of portals.

Mycetoma (Actinomycotic) Duration Thirty Years. Presented by DR. MOLLEURUS COUPERUS and (by invitation) DR. DONALD S. FREIBURGER.

During the last 22 years, a 69-year-old man, born in Guanajuata, Mexico, has handled "Arizona clay," which is used for filtering petroleum products. Prior to that time he did construction work with concrete. He says he has never worked barefoot.

The patient has been living in the United States all the time (with the exception of a one-month visit to Mexico in 1956) since 1916. He lived in Mexico before 1916.

He injured his right foot with a pick-axe in 1928. Approximately six months later, he was treated at a Los Angeles hospital for "mycetoma, right foot" by "excision of mass." (See slide No. 8909, dated April 18, 1929.) In 1945 he had a second operation performed at another Los Angeles hospital because of a "knot" on the dorsum of his right foot. This operation resulted in subjective improvement, although the foot remained somewhat swollen and deformed. Since 1953 the swelling has increased gradually and the patient has noted occasional pain on the dorsum of the foot. He has remained ambulatory since onset of the disease.

The right foot is grossly swollen and deformed, especially the distal three-fifths and the first four

toes. There is some induration. Several recently draining areas are evident on the dorsum. Sometimes a little dorsal tenderness can be elicited.

Biopsy findings (see slides No. 5489, December, 1957, and No. 8909, April 18, 1929): 1. Hematoxylin and eosin, Gram, and Hotchkiss-McManus stains: (*a*) granulomatous lesion in dermis; (*b*) granule ("ray fungus"). 2. Gram stain: granule comprised of small branching filaments consistent with Actinomyces bovis and Nocardia.

Other significant laboratory findings: 1. Blood: Hgb. 15.5 gm. (103%); WBC 10,000 (16L, 4M, 1E, 2B, 77N); platelets: est. normal. 2. Urinalysis: not remarkable. 3. Serologic test: negative. 4. Chest film: normal. 5. X-ray films of feet: normal bones. 6. Glucose-tolerance test (three-hour oral): normal. 7. Bacteriology: Smear, culture, and sensitivities of purulent material from lesion reveals Micrococcus aureus (β-hemolytic, coagulase-positive) sensitive to all antibiotics and chemotherapeutic agents except Gantrisin, sulfadiazine, sulfamerazine, Triple Sulfa, Thiosulfil, Elkosin, and streptomycin. 8. Mycology (see slides): (*a*) Crushed granule from lesion: Gram stain reveals small Gram-positive branching filaments consistent with Actinomyces bovis and Nocardia; no spores seen. (*b*) Thioglycollate broth: (1) Gram stain of smear of anaerobic growth reveals small gram-positive branching filaments consistent with Actinomyces bovis. (2) Ziehl-Neelsen stain reveals that the small branching filaments are not acid-fast. (*c*) Sabouraud's dextrose agar: no filamentous growth.

Discussion

DR. J. WALTER WILSON: I was very much pleased to see this case and to note the diagnosis of actinomycosis of a foot due to A. bovis, because I have elected in both of my books to consider what is usually called madura foot or mycetoma as a part of actinomycosis. In my opinion, it is the same clinical syndrome as actinomycosis except that it is in a different part of the body. It is true that actinomycosis due to A. bovis occurs usually in the areas of the throat, the neck, the teeth, sinuses, and the intestinal tract, because that is the habitat of that organism. As it is not common to find A. bovis in a foot one could wonder how it got there, particularly from an injury with a pickaxe, as in this case, since it is not to be found in soil. There are recorded cases of A. bovis infection of arms and legs due to animal or human bites, and I asked this man particularly whether he had ever been bitten by an animal. I think also we can learn something else from this man. He can walk—not entirely well, admittedly, but he is able to walk, even though his foot has been involved with this disorder for 30 years. We should wonder whether this man was not wise after all when he wouldn't let the surgeons amputate. Sometimes this condition continues notoriously chronic for years without interfering with the life of the patient. It certainly is not a systemic health problem. I also was glad to meet this patient, because he is probably the only person who has lived as long as he has in the United States who hasn't had penicillin. He said he had had no more than three injections of anything in his lifetime. The cultures revealed an organism sensitive apparently to penicillin. This is additional evidence for A. bovis because it is sensitive to penicillin more than to sulfonamides. I believe this man should be given large amounts of penicillin.

DR. JEROME K. FISHER: Is this a suitable case for amphotericin B?

DR. J. WALTER WILSON: Dr. Victor Newcomer can tell you more about it than I can. Until we are more certain that amphotericin will not have any more toxic effects than we know of at the present (I refer to toxic effects that might not show up in the first year or so after a sufficient amount of such a drug has been used), I think we should probably withhold it, particularly from patients who get along as well as this one has.

DR. MOLLEURUS COUPERUS: Dr. Freiburger did the work-up on this patient, and he will close the discussion. The same problem regarding the origin of the infection which troubled Dr. Wilson also troubled us. The fact that the patient received this injury with a pick while working on a sewer in Los Angeles makes it, at least theoretically, possible that the Actinomyces was carried by the sewage and that the patient obtained his infection that way.

DR. DONALD S. FREIBURGER: I think that the most interesting aspects of this case are its long duration, 30 years by history and 29 years histopathologically, and the fact that the patient has no bone damage in his foot. As far as treatment is concerned, it will depend upon the mycological diagnosis. We must decide which drug to use to combat the causative organism. We have ruled out the higher fungi and botryomycosis and believe that the organism is either Nocardia or A. bovis. It is most likely Actinomyces. Choice of a drug is not the only consideration, however. Are we going to do a surgical procedure? If so, what kind? I believe we will have to administer drugs, penicillin, or some other antibiotic or chemotherapeutic agent, and, after a certain period of time, perform a conservative surgical procedure, immobilize the patient perhaps and then continue the drugs postoperatively. This type of program was suggested by Dr. W. P. Cockshott last year in the *West African Medical Journal* (The Therapy of Mycetoma, 6:101-107, 1957). His article outlines a program of medication and conservative

surgery followed by more medication and immobilization. I want to mention one more interesting thought from his article. Bone and joint tuberculosis with secondary infection and sinus formation formerly was treated almost exclusively by surgery, usually by amputation or some other relatively radical operation. Today it is being treated successfully with less radical surgery in combination with antibiotics. He suggests that mycetoma might eventually fall into a similar class therapeutically.

Case for Diagnosis: Lymphoblastoma; Variant of Sulzberger-Garbe Syndrome? Presented by DR. NORMAN E. LEVAN.

Lichen Planus of the Palms and Generalized. Presented by DR. ROBERT L. DAY.

Case for Diagnosis: Lichen Planus? Presented by DR. ROBERT L. DAY.

Parapsoriasis en Plaque with Poikiloderma-like Changes: Prob. Early Mycosis Fungoides. Presented by DR. JEROME K. FISHER.

Lymphocytoma Cutis. Presented by DR. MURRAY ZIMMERMAN.

Raynaud's Syndrome, with Gangrene of Fingertips. Presented by DR. NORMAN E. LEVAN.

Mycosis Fungoides. Presented by DR. JOHN D. ROGERS.

Discoid Lupus Erythematosus. Presented by DR. JEROME K. FISHER.

MINNESOTA DERMATOLOGICAL SOCIETY

Harold Ravits, M.D., President

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Oct. 24-26, 1957*

Lichen Planus? Leukemia? Carcinoma? of the Tongue.

Presented by DR. FRANCIS W. LYNCH.

A 33-year-old white man has noted a persistent lesion on his tongue for the past 13 years. The patient was examined at the Mayo Clinic in 1944, and a diagnosis of lichen planus of the tongue was entertained. He noted a lesion on his lower lip in 1956. Pathologic examination of a biopsy performed on the lip lesion in 1957 showed changes diagnostic of squamous-cell carcinoma. A surgical excision of the carcinomatous area was performed.

Physical examination reveals involvement of the dorsum of the tongue with thickened papules and plaques.

Discussion

DR. HAMILTON MONTGOMERY, Rochester, Minn.: In this case I believe Herman Beerman thought he saw some carcinoma in one of the sections, but I saw pseudoepitheliomatous hyperplasia and the picture of lichen planus in the other section.

DR. HERMAN BEERMAN, Philadelphia: I thought I saw some epitheliomatous change, but I will admit that is is probably pseudoepitheliomatous, and lichen planus basically. Clinically, I thought this patient has a geographic tongue. He said it varies from time to time.

DR. HENRY MICHELSON, Minneapolis, Minn.: The treatment is a problem here. Having accepted the diagnosis of lichen planus, which I think it is, then what's next? No one had cautioned the patient about smoking. I don't think he should be allowed to smoke. You'll think I'm a fanatic about this tobacco business, but I do believe that when there is anything wrong in the mouth one should not smoke. Now then, what to do? I think that all lichen planus of the mouth is entitled to a trial with the stock empiric drugs, whether it be mercury or bismuth or a chloroquine, Plaquenil, and Atabrine mixture, and painting with trichloracetic acid is worthwhile.

DR. STEPHEN ROTHMAN, Chicago: I am sorry that I disagree with the opinion of Dr. Michelson. I believe that none of the recommended procedures is effective in treatment of lichen planus of the mucous membranes. Our statistics have shown that bismuth is entirely ineffective. Caustic or abrasive local measures will cause much pain, but I doubt it will prevent recurrences. The harmful effect of smoking remains to be proved. Psychologically, I fully agree, most of these patients are carcinophobes. But I am convinced that carcinophobia is only nurtured by active treatment, particularly if it is ineffective. One should be firm in stating that this is a benign condition and has nothing in common with leukoplakia except the white color.

DR. ANTHONY CIPOLLARO, New York: I hate to get off again on this, but I asked Dr. Michelson to discuss the treatment because I think this is where the dermatologist has a terrific responsibility to the patient. Now this person has lichen planus. No question about that diagnosis. But—this is an active disease on the tongue. The tongue

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is a site where cancer develops easily and frequently, and I think that we have to take a very active attitude toward this person regardless of what his psyche is. We have to keep him under good control; some mouth hygiene, no smoking, vitamins, things of that sort should be administered to this patient, and he should be examined extremely carefully each time he comes in, for this type of soil is favorable for the development of cancer.

DR. CLARK FINNERUD, Chicago: I just arrived here, and so I do not know what has been said about Case 1, but a point I want to bring out is the fact that, although leukoplakia and lichen planus of the mouth are entities, it may be practically impossible to decide between the two clinically. When that is true, it commonly is also true histologically. In this instance, although I am sure some will disagree, I favor the diagnosis of leukoplakia. Leukoplakia of the tongue is rare in the absence of involvement of the buccal mucosa. I might mention, incidentally, that lichen planus of the mouth sometimes responds favorably to bichloride of mercury paintings, for which Dr. Michelson gave me the formula many years ago. We all realize that almost nothing is more resistant to treatment than lichen planus of the mouth. However, as stated, we have used this locally with some success, with and without employing internal measures.

DR. FRANCIS W. LYNCH, St. Paul: The management of this patient has been a problem principally because the patient has been very confused as a result of his medical advice. I have felt that he definitely has lichen planus and that the risk of developing oral cancer in this case is minimal. However, others have told him that he has leukoplakia and, as a result, he had excision of a considerable portion of the surface of the lower lip. A general pathologist made a diagnosis of cancer of the lip. I thought the reaction to be nonepitheliomatous hyperplasia. I am glad to have the opinions of this group so that I can reassure the patient.

Scleroderma? with Hemiatrophy. Presented by the Staff of the University Hospital.

A 6-year-old white girl has had a circular area of alopecia anterior to her right ear since birth. For the past 18 months the patient has experienced a flattening of the structures of the right side of her face. This appeared to follow an infection of this area with edema of the right eye. Her general health has been good except for frequent attacks of otitis media. The patient has been admitted to the University Hospital on two occasions for study of the present condition but has received no therapy.

On physical examination the skin and subcutaneous tissue of the right cheek, nose, and jaw are noted to be sclerotic and atrophic. There is a firm circular area of alopecia anterior to the right ear. The right mandible appears underdeveloped, producing a marked asymmetry of the face. There is slight muscular atrophy of the right lateral border of the tongue and a deviation to the right on projection of the latter organ.

Roentgenograms revealed an underdevelopment of the mandible on the right, slight right maxillary sinus mucosal thickening, and a normal vertebral column. Pneumoencephalogram showed a large indentation of both lateral ventricles, probably due to a large calcar avis.

Pathologic examination of a cutaneous biopsy performed on the right cheek revealed changes compatible with, but not diagnostic of, scleroderma.

Skin temperature studies have demonstrated a sympathetic-parasympathetic imbalance with probable sympathetic preponderance.

The patient will receive a trial on parasympathetic drugs under the direction of the department of physical therapy.

Generalized Scleroderma. Presented by DR. JOHN G. RUKAVINA.

A 34-year-old white woman noted the onset of an aching shoulder pain two years ago, followed by a similar involvement of the small joints of the hands, feet, knees, and elbows. At the same time she noticed color changes (purple and white) upon exposure of the digits of her hands and feet to cold. One year ago the patient experienced the onset of stiffness and loss of sensation over the left cheek, tightening of the skin, decrease in function of the fingers, and difficulty in walking up stairs. There has been no weight loss, dysphagia, or digital ulceration.

The patient was studied at the Mayo Clinic in February, 1957. Muscle and cutaneous biopsy performed at that time on the right deltoid region revealed changes compatible with a diagnosis of scleroderma. Electromyography, electroencephalography, and an L. E. clot test were normal.

The diagnosis of scleroderma, with elements of dermatomyositis, was entertained, and it was suggested that she be started on corticosteroids. The patient has been maintained on oral cortisone (100 to 62.5 mg.) by her family doctor for the past five months, with a response of decreased joint pain and a feeling of well-being. She has been without cortisone for one week and has noted increased joint pain and swelling.

The patient was admitted to the University of Minnesota Hospital on Oct. 14, 1957, for further study and intravenous chelation (EDTA) therapy.

Physical examination reveals bilateral pupillary membranes (result of a cataract operation at the

age of nine years); slight tightening of the skin on the dorsae of the hands and digits, forehead and cheeks; poor pedal pulses; slight drooping of the left corner of the mouth; hypesthesia over the distribution of the left lower trigeminal nerve and generalized weakness, without muscle atrophy, greatest in the upper extremities.

Significant laboratory data reveal C-reactive protein 3+; total protein 7.8 gm. % with albumin 2.9 and globulin 4.9 gm. %; normal urinalysis and L. E. clot test, normal roentgenograms of the gastrointestinal tract, chest, teeth, and involved joints.

A cutaneous biopsy performed on the right forearm reveals changes compatible with early scleroderma.

The patient has received daily intravenous infusions consisting of 3 gm. of EDTA in 500 cc. 5% dextrose in water.

Discussion

DR. LOUIS BRUNSTING, Rochester, Minn.: The occurrence of hemiatrophy with morphea and scleroderma in childhood I believe is the rule rather than the exception. The two conditions do not always appear at the same time, as was shown here. These findings point to some involvement of the nervous system in the background, with the changes in the skin being secondary. The point is emphasized also in acrosclerosis in adults, where there is uniformly a disturbance of the sympathetic functions with Raynaud's phenomena. In our hands the use of treatment by chelation brings about a considerable loss of calcium through the kidneys, but the subjective improvement in the sclerodermatous stage leaves much to be desired. Dr. Sigfrid Muller has been following these patients closely and may wish to comment.

DR. SIGFRID MULLER, Rochester, Minn.: We have treated about 11 or 12 patients with scleroderma, a few with generalized morphea, and a few with acrosclerosis. Their ages have varied from about 18 to 65, and the duration of sclerosis about 15 years in a couple of patients, and in the rest it was of relatively brief duration, usually less than two years. Our results have not been too good, and, consequently, I haven't been to enthusiastic. However, in a couple of patients there seemed to be considerable improvement, especially in the edematous phase of scleroderma. It is extremely difficult to evaluate, because all the patients tell you they are better, although you can't judge it to be so by feeling their skin. One of the problems has been to establish definite criteria by which we can judge whether we have improvement, objective improvement, or whether it is subjective.

DR. CARL LAYMON, Minneapolis: I merely wish to ask Dr. Muller a question. What does he mean by generalized morphea?

DR. SIGFRID MULLER, Rochester, Minn.: By generalized morphea I mean limitation of the sclerosis to the skin, with a widespread distribution, without involvement of other organs.

Systemic Moniliasis. Presented by the Staff of the University Hospital.

A 3-year-old white girl had been in good health until the age of 10 months, when she experienced the onset of a scaly eruption concentrated in the inguinal and presternal areas. The condition cleared rapidly under the use of mycostatin ointment. At the age of 12 months the patient was admitted to the University of Minnesota Hospital because of complaints of diarrheal stools, fever, and failure to gain weight. At that time, because of fatty stools, duodenal x-ray patterns and deficient fat and vitamin A absorption, the patient received a diagnosis of celiac syndrome and was placed on a celiac diet. In addition, reversal of the albumin-globulin ratio and normal serum calcium and phosphorus were noted. Intestinal symptoms have not been present since the age of 14 months, though the patient has been on a varied diet.

At the age of 17 months the patient's parents noted persistent white spots in her mouth and brown scaly lesions on her shoulders, neck, and genitalia. The eruption disseminated to the forehead, scalp, and axilla, and in its entirety was waxed and waned since the time of onset. The patient has had six additional University Hospital admissions for repeated episodes of upper respiratory infections, bronchopneumonia, unexplained febrile episodes, and therapeutic trials for her cutaneous condition.

She has received trials on oral preparations of nystatin (Mycostatin), amphotericin B, vitamin D, estradiol-progesterone combination, colostrum, and, at present, diiodohydroxyquin (Diodoquin). Topical Vioform, zinc undecate (Desenex), amphotericin, Castellani's paint, nystatin, and gentian violet have been applied. Temporary regression of the eruption was noted with the use of amphotericin B. The most rapid regression has occurred in the past three weeks concomitant with the use of oral Diodoquin.

Laboratory studies have revealed a persistent unexplained alkaline phosphotase elevation; a persistent reversal of the albumin-globulin ratio; repeated cultures of Candida albicans from the nose, throat, feces, skin, nails, and occasionally vagina; numerous mycelia in the upper epidermis on a cutaneous biopsy, and a low-normal height-growth curve.

Physical examination reveals crusted papules and plaques on the scalp, cheeks, chin, ears, axillae, neck, and trunk. There is a polycyclic border with central clearing in the right axillary plaque. White adherent patches are present on the tongue and

buccal mucosae. Erythematous-squamous patches are seen on the digits of the hand with hypertrophy of the right third and left first and third digital nail plates. An erythematous plaque on the inguinal and perineal areas is also noted.

Discussion

DR. JOHN H. LAMB, Oklahoma City: I think that Dr. Rothman should open this discussion, since he has reported a case with hyperkeratotic granulations due to Candida albicans. We had a severe case of Monilia infection of the oral mucosa and entire gastrointestinal tract which in the early stages was very much like this one. However, the keratotic granulations on the skin and nails were due to Microscoporon canis and not Monilia. Our patient died at the age of 18 years of starvation, loneliness, and inanition. We tried many forms of treatment, all of which failed. I don't have any recommendation for treatment in this case.

DR. STEPHEN ROTHMAN, Chicago: I agree with Dr. Lamb that this baby's condition corresponds with what Dr. Hauser and I described as Monilial granuloma. Our patient died in diabetic coma. A second patient we had an opportunity to observe had a profound pancreatic digestive deficiency. Thus, it seems probably that pancreatic disease is the primary condition from which Monilial granuloma develops. Acrodermatitis enteropathica seems to be an entirely different entity. This disease is primarily a disease of the small intestines and can be cured by administration of Diodoquin. I am surprised to hear that this baby has done well with Diodoquin. If so, there might be some relationship between Monilial granuloma and acrodermatitis enteropathica. On clinical grounds I would be reluctant to accept any relationship between these two diseases. Dr. Cipollaro has published one of the most characteristic cases of monilial granuloma, and maybe he would comment.

DR. ANTHONY CIPOLLARO, New York: So far, the speakers have not emphasized the fact that this child has celiac disease, and I think that is what makes it difficult in trying to get a response to the monilial infection. Now, ordinarily moniliasis is not too servere a problem, even generalized moniliasis, but when the patients develop granulomas there is always a systemic background, just like—well, this particular patient has celiac disease. Last year I had a case similar to this, only the moniliasis was 10 times worse than you see here, large granulomatous lesions all over the scalp and on various parts of the body. The patient had a great big stomach that the pediatricians diagnosed as celiac disease, and the combined talents of the dermatologists and the people interested in metabolism and the pediatricians were not able to do much with this child. The child died after having had the disease for about a year. Now, the question of acrodermatitis enterohepatica—that is a rare disease. We have one in New York that has been shown at various meetings. This child has terrific diarrhea and a dermatitis mostly of the extremities resembling epidermolysis bullosa. Lesions are also present around the knees. The diarrhea is very severe when the cutaneous lesions are most active. A few doses of Diodoquin clears this child right up. Now there must be some similarity in this group of diseases. They must be systemic diseases with involvement of other organs.

Pustular Psoriasis? Presented by the Staff of the Minneapolis Veterans' Hospital.

A 31-year-old white male truck driver, noted progressive joint pain in June, 1952, which began to involve the ankles, knees, hips, back, and shoulders. In July, 1953, the patient noted a penile discharge, followed in one month by a scaling, elevated eruption, involving the soles, scalp, and nails. At this time he also had oral ulcerations, conjunctivitis, and balanitis. The patient was treated initially with a short course of cortisone, penicillin, and streptomycin for rheumatoid arthritis and then was transferred to a California Veterans' Hospital, where a diagnosis of Reiter's disease was made. Within six months the skin was completely clear and the only residue of this disease consisted of periodic episodes of mild arthralgia.

The patient remained well until June, 1957, at which time he noted the onset of ankle pain, accompanied by an elevated, papular eruption on the extensor surfaces of the forearms. Over a four-week period the eruption spread to involve all body surfaces except the central face and palms. Destructive nail changes and mild oral ulcerations began at the same time. The patient was admitted to the Minneapolis Veterans' Hospital on Aug. 27, 1957.

Physical examination reveals sharply demarcated, crusted plaques on all surfaces of the body, except for the face and palms; shallow ulcerations on the labial and buccal mucosa, and generalized lymphadenopathy.

Laboratory study was within normal limits except for two sedimentation rates, which were reported as 66 and 85 mm. in an hour, respectively, and two white blood cell counts which showed moderate leukocytosis with a moderate shift to the left. Roentgenograms of the feet demonstrated a small cystic area at the distal end of a phalanx of the foot and soft tissue swelling above the left ankle.

The patient was treated with oral salicylates and petrolatum to all areas, except the scalp,

where he used half-strength Sal-Sulfur for seven days. At a later date the patient was given penicillin parenterally and ammoniated mercury and bacitracin ointment topically. Three and one-half weeks after admission, cortisone (200 mg. a day) was prescribed, with rapid improvement noted.

Discussion

DR. HERMAN BEERMAN, Philadelphia: I don't know what pustular psoriasis is, but I thought this patient's constitutional complaints and history suggested Reiter's syndrome, in which lesions are very similar to those one sees in keratodermablennorrhagica. This is histologically, I believe, psoriasis with huge Monro's abscesses. I bow to Dr. Michelson's possible diagnosis.

DR. HENRY MICHELSON, Minneapolis: This patient has been on our service at the Veterans' Hospital, and I have been intensely interested in him because I have been trying to get together a paper on unusual psoriasis. I think that in psoriasis particularly we have three histologic features from which we can build up psoriasis any way we want to—the hyperkeratosis, the infiltrate in the corium, and in the pustule of the Monro abscess. When Professor Pincus was here and we were discussing psoriasis he brought something to my attention that I didn't realize. We always think of an abscess as being round. Pincus brought out that a Monro abscess may be perfectly flat, and, therefore, you may call a collection of pus an abscess when it is flat. It doesn't have to be round to be an abscess. In this case you see where this abscess, if you want to call it that, elevated itself, migrated to the surface, and became a large, flat abscess. Now then, this question comes up: Reiter's disease versus pustular psoriasis. Reiter's disease is not a very clearly defined entity. One thing that we have seen in all the Reiter's cases we have had—and we have had a lot of them—30 or 40 cases—is that there is a profound loss of weight; there is pain, high temperature, long-lasting, but it comes to an end within two or three months. This man has had psoriasis or psoriasiforme attacks again and again, and when we saw him this time we felt that he had undeniable symptoms of psoriasis and he also has some symptoms of Reiter's disease. But in the Reiter's part of it—the mucous membrane, the urethritis, the lack of conjunctivitis and mild arthritis—I believe we are dealing with what Zumbusch first described as psoriasis pustulosa. And I think this answers that description very well.

Multiple Leiomyomas. Presented by the Staff of the University Hospital.

A 54-year-old white woman noted the onset of tender nodules on her back and arms 27 years ago. The lesions have gradually increased in number but not in size. The nodules have not been spontaneously painful, nor have they been affected by temperature changes. One of the patient's nine brothers has similar lesions on his arms and back.

Physical examination reveals grouped pink, tender nodules on the scapular and sacral areas and diffuse similar nodules on the extensor aspects of the upper extremities. The lesions are not affected by the application of heat or cold.

Pathologic examination of a cutaneous biopsy performed on a nodule on the arm reveals changes diagnostic of leiomyoma.

Discussion

DR. CLARK FINNERUD, Chicago: The younger men present today are fortunate in having seen here a classical case of this entity. I was in dermatology for many years before I first saw a patient with this disorder, and then I encountered three within a week or so. Once seen, it is never to be forgotten, in that probably 9 out of 10 such cases follow the same pattern—pea to navy bean size, oval and round nodules, usually slightly reddish, with or without subjective symptoms, and occurring in groups. Although the case is usually clinically typical, of course for the record we perform a biopsy, and for differentiation we use Van Gieson's stain.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. Winkelmann and I have been studying a large group of myomas of the skin, some of them classical leiomyomas, some with pain and some without pain. Then there are also deeper lesions, namely, angiomyomas that arise from the smooth muscle of the walls of blood vessels, in contrast to the more superficial leiomyomas that are arising from the arrectores pilorum muscles. It would seem that a myoma is painful when it extends down into the subcutaneous tissue. Then there is the so-called dartoic myoma that usually occurs in the dartoic muscles of the scrotum.

Xeroderma Pigmentosum. Presented by the Staff of the University Hospital.

A 30-year-old mentally retarded white man has experienced cutaneous and conjunctival sensitivity to the sun's rays since birth, with cutaneous erythema and blistering and conjunctival injection subsequent to such exposure. The patient has had numerous keratoses and basal- and squamous-cell carcinomas on the lips, face, ears, and neck since the age of 12 years. Treatment of these lesions has consisted of irradiation and surgical excision. The patient has lived at the Faribault School for the past 12 years. His older sister, who was similarly affected, died as a result of intestinal obstruction at the age of 33 years.

Physical examination reveals numerous telangiectasias, ephelides, and depigmented scars on the face and neck. The patient's nose is distorted by scar tissue. There are leukoplakic patches on his lower lip and scattered on the alveolar ridges. Bilateral conjunctivitis is present. There are ephelides and punctate keratoses scattered over the extensor aspects of his arms and on his scapular region. Several verrucous nodules appear on the third digit bilaterally.

Numerous Basal-Cell Epitheliomas, Arsenical Keratoses, and Chronic Eczema. Presented by Dr. Francis W. Lynch.

A 54-year-old white man has had recurrent episodes of eczema since the age of 7 years. For the past 17 years he has had numerous keratoses on the palms and epitheliomas on the face. There is no definite history of arsenical ingestion. The patient received a course of BAL at the University Hospital in 1947. His many epitheliomas have been treated by irradiation (40), electrosurgery (several hundred), or plastic surgery (left cheek).

Physical examination reveals numerous keratoses on the palms; epitheliomas predominating on the right cheek, posterior neck, and left infraorbital area, and evidence of a disseminated neurodermatis (atopic eczema).

Pathologic examinations of specimens from repeated biopsies performed on facial lesions have revealed changes diagnostic of basal-cell epitheliomas.

The patient is presented with the diagnoses of unusually numerous basal-cell epitheliomas, arsenical keratoses, and chronic eczema.

Squamous-Cell Carcinoma of Chin (Skin and Mandible) with Nocardia Madurae Infection (Mycetoma?). Presented by the Staff of the University Hospital.

A 49-year-old Montana rancher fell off a horse five months ago and sustained a lesion on his chin. The patient was examined at a Montana clinic six weeks ago because of the persistence of the lesion. A biopsy performed at that time revealed changes diagnosed as squamous-cell carcinoma. A roentgenogram showed an osteomyelitis of the mandible. The patient received irradiation to the chin (1400 r over a three-day period) and was subsequently referred to the University of Minnesota Hospital. He has had no systemic symptoms and has not lived outside the state of Montana. In 1953 he received an unknown amount of irradiation for a cancer on his nose.

Physical examination reveals a 6×3 cm. scarred patch, with crusting at the superior pole, on the right side of the nose and a narrowed sclerotic right nasal cavity. A 6×4 cm. indurated tumor, with deep attachment, involves the central mandibular and submental areas. A small central ulcer puts forth an intermittent seropurulent discharge. There is no other lymphadenopathy or positive physical finding.

Culture of the chin exudate on varied media revealed the presence of Nocardia madurae.

Biopsies performed on the chin revealed changes compatible with the diagnosis of squamous-cell carcinoma (pseudoepitheliomatosis hyperplasia had been considered); while that performed on the crusted area on the nose showed changes diagnostic of basal-cell epithelioma.

Roentgenograms of the mandible demonstrated an inflammatory or neoplastic bone irregularity.

A mandibular bone biopsy showed changes diagnostic of squamous-cell carcinoma.

Mycologic study of the latter area has demonstrated no pathogen after five days.

The patient has received 63 gm. of sulfadiazine over a two-week period with no appreciable change. He is to be admitted to the surgical service for an excision of the involved skin and mandible, a suprahyoid dissection, and a plastic repair. The basal-cell carcinoma of the nose will be irradiated at a later date.

Discussion

Dr. Cornelius F. Lehmann, San Antonio, Texas: There is a question of treatment in the case with multiple epitheliomas and arsenical keratoses. I think in most instances, in a case like this, that electrosurgery or cautery would be the most preferable and most practical. I wouldn't put irradiation as first, because I think that with the history of arsenical ingestion one is going to have a lot of sclerosis in that skin eventually, which means the vascular bed would not be so good. This means that following irradiation you're going to have more atrophy, more atrophic scarring, and breakdown later if he lives long enough. The case of mycetoma with carcinoma is of interest to me. I think before definite cancer therapy is given him he should be treated, that is, the infection should be treated very drastically. He has only had sulfadiazine for a two-week period. He has probably had this lesion for a very much longer period of time, and the question in my mind is which is of the greater moment. Right now, I would say that the nocardial infection is the paramount issue. At a later date, after, when, and if that inflammatory induration doesn't go down, I think the treatment of choice there would be an operation.

Dr. John Lamb, Oklahoma City: In regard to the case of nocardiosis of the chin, I agree with Dr. Lehmann that this looked more like actinomycosis than it did carcinoma. I have never seen a Nocardia infection involved along with a malig-

nancy, nor did we ever find Nocardia in our cervical-facial actinomycosis cases. I thought the culture presented looked like a Nocardia. It had not yet turned red as we see in Nocardia madurae, and it has no musty odor which is usually found in the Streptomyces groups. Since no granules have been found in the granuloma, we would even suspect an acid-fast type. We have had two cases of mycetoma of the feet, in Oklahoma. One was an infection with Nocardia asteroides which was acid-fast, in a young girl, due to an injury from a garden tool. The other case was a long, chronic mycetoma due to N. madurae; this was non-acid-fast. Several dermatologists who have been to Mexico City state that several cases of acne conglobata were presented from which Nocardia had been isolated. In the therapy of this case I would suggest the use of streptomycin over a long period of time. We have used it in our case of Nocardia madurae and after about three weeks the abscesses have stopped draining for the first time in several years. The patient received a dose of streptomycin of 0.5 gm. twice daily. I would like to ask a question about the case of xeroderma pigmentosa. I wondered whether the psoralens or the antimalarials had ever been tried in these cases. We feel that the antimalarials have helped some of our severe cases of farmer's and sailor's skin in Oklahoma.

DR. HENRY MICHELSON, Minneapolis: I want to make one comment in answer to Dr. Lamb. There was a very nice study done on xeroderma pigmentosum. I can't recall the article at the moment, but it showed that xeroderma pigmentosum lesions could be provoked not only by sun's rays but by x-rays and many other agents. Therefore, this disease is a constitutional defect that isn't dependent entirely on light sensitivity. I was expecting Dr. Brunsting to say something; we have been interested to know whether this disease is related to, or in any way could be associated with, so-called erythropoietic or congenital porphyria. The diseases are similar, but these patients survive longer than the congenital porphyria group and they do not have the other characteristics. I don't believe that anyone has ever found porphyria in xeroderma pigmentosum.

DR. LOUIS BRUNSTING, Rochester, Minn.: I do not know of any case of xeroderma pigmentosum in which abnormal porphyrin metabolism has been demonstrated. The only resemblance to erythropoietic porphyria in childhood is in the appearance of the skin and the photosensitivity, which are unexplained.

DR. FRED MOHS, Madison, Wis.: At University Hospitals at Madison we had an interesting case of xeroderma pigmentosum in a boy who, between the ages of 3 and 15 years, had nearly 50 basal- and squamous-cell carcinomas. Of these, 28 were removed chemosurgically and now, at age 25, the patient has been free of cancer for 10 years. Since no new cancers have appeared during this time, the possibility is suggested that, if the patients can be carried to a certain age, they may tend to outgrow the condition. Perhaps this observation may be a clue to the causation of the disease, and it may stimulate further research on the subject. A similar observation occasionally is made in cases of multiple basal-cell carcinomas. I have over a dozen patients who come from various parts of the country at intervals of once or twice a year for removal of a new crop of these neoplasms. Over a period of several years we may remove as many as 200 cancers from a single patient. Finally, however, the tumors appear with decelerating frequency, and at each visit fewer and fewer are found. Hence, the condition is not as discouraging as we originally may have thought. With regard to the treatment of the patient with the multiple lesions on the face, I should use the chemosurgical method with the full microscopic control. However, for multiple superficial lesions on the trunk this microscopic control is unnecessary. The lesions are simply shaved off very superficially and the bleeding is stopped by the application of dichloracetic acid. This chemical makes the cancer tissue turn white so that it stands out against the grayish background of the cauterized dermis. Thus, with a good magnifying loupe it is possible to see any residual foci of cancer. The excision and cauterization is repeated, if necessary, until the area is grossly cancer-free. The results with this treatment of these relatively benign superficial lesions of the trunk have been excellent, but this is the only type of malignant neoplasm that we treat without the complete microscopic control which may be obtained with the chemosurgical method. More deeply invasive lesions, even though on the trunk, require microscopic guidance, as do all lesions on the face because of the frequency of unpredictable extensions from the main mass of these cancers. With regard to the last case of squamous-cell carcinoma with an associated Nocardia infection, there is a choice either of radical surgical resection along with a portion of the mandible or of chemosurgical excision. If the latter method were used, and if there were not appreciable invasion of the bone, it might be possible to preserve the continuity of the mandible. The main mass of the cancer would be cut out surgically, following which the chemosurgical excisions would be carried out till a microscopically cancer-free level was reached. The fixative chemical would kill the Nocardia organisms as well as the carcinoma cells. In the process of removing the carcinoma extending along the mandible, a thin layer of bone would be killed by the chemical and this layer

would separate in about three weeks. Carcinomatous invasion of the bone would produce pitting and honeycombing which would be visible grossly but which could be checked microscopically with frozen sections. After separation of the layer of fixed bone, a repair of the defect could be carried out immediately or it could be delayed for a few weeks if desired. The patient with basal-cell carcinoma that was showing activity after radiation treatment would be a good candidate for chemosurgical treatment. In such a case, we would not be at all surprised if there were extensions into the radiation scar and for some distance into the tissues at the periphery. The extent and location of these "silent" outgrowths can be determined accurately by the microscopically controlled excisions which characterize the chemosurgical method.

DR. STEPHEN ROTHMAN, Chicago: In connection with what Dr. Michelson has said it is interesting to note that Gougerot as early as 1920 suggested that xeroderma pigmentosum may represent hypersensitivity to cosmic rays. However, I do not know of a single case in which lesions would have appeared on covered parts of the body. With sensitivity to hard ionizing radiation, of course, it would make little difference whether one wears garments or not. In one of my cases test irradiations with ultraviolet rays did not show decreased erythema threshold but telangiectases developed in the irradiated area, a definitely pathological reaction. Nobody has yet established the action spectrum of ultraviolet in xeroderma pigmentosum. With today's powerful monochromator instruments this would not be a difficult task and should be done. Xeroderma pigmentosum has nothing in common with congenital porphyria, except that both are destructive diseases. Congenital porphyria is a Mendelian dominant; xeroderma pigmentosum, a Mendelian recessive. Abnormal porphyrins never have been shown to occur in xeroderma pigmentosum. In this case I was unable to find out whether there was consanguinity in the parentage. It would be interesting to know.

DR. FRANCIS LYNCH, St. Paul: In the case of the patient with xeroderma pigmentosum there was no familial history of consanguinity. A sister had a much severer example of the disease and was the subject of some investigative studies on my part more than 20 years ago. The patient presented today has been an inmate of a state institution because of his mental status, and thus he has had a minimum of exposure to sunlight throughout the years. His cutaneous involvement has increased in severity so slowly that we have no difficulties dealing with it. The patient with multiple basal-cell epitheliomas has strongly objected to electrosurgical treatment with local anesthesia but does submit to periodic treatment by electrosurgery for numerous lesions under general anesthesia. During the periods between these treatments we have treated occasional single lesions with roentgen radiation. In recent years the number of new lesions seems to be somewhat less than before, whether because of the BAL or because of the natural course of the illness cannot be determined at this time. In presenting him we had in mind the possibility of discussion of chelation therapy.

Kaposi's Hemorrhagic Sarcoma. Presented by DR. S. E. SWEITZER.

Kaposi's Idiopathic Hemorrhagic Sarcoma. Presented by the Staff of the University Hospital.

Discussion

DR. ROBERT GOLTZ, Minneapolis: Dr. Sweitzer would be particularly interested in any comments that might be made about β-irradiation treatment for Kaposi's sarcoma. Has anyone any information on that?

DR. ANTHONY CIPOLLARO, New York: Both cases are quiescent, and in this stage I see no real necessity for treatment. Compression bandages should be applied if edema develops. If tumors or large angiomatous lesions develop, they should be treated with x-rays individually. The whole leg doesn't have to be treated. Of all the methods of treatment that I've used in Kaposi's sarcoma I found that x-rays have been the best. There is a time in Kaposi's sarcoma when the leg becomes edematous and ulcerations develop. The lesions fail to respond to x-ray therapy. Some of the cases from New York have gone up to Boston to have the cathode-ray treatment with good results. Of course, there isn't anything permanent about that type of treatment any more than with conventional x-ray therapy.

DR. JOHN SCHMID, Duluth, Minn.: In 1948 a patient with severe Kaposi's sarcoma, namely, ulcerating granulomas and elephantatic edema of the hands and feet, was treated with nitrogen mustard. The response was most gratifying, in that antibiotics, radiation, and local treatment had reached an impasse.

Disseminated Lupus Erythematosus. Presented by the Staff of the Minneapolis Veterans' Hospital.

A 28-year-old white male carpenter was admitted for the first time to the Minneapolis Veterans' Hospital in February, 1955, with symptoms and signs of six months' duration. The condition began with erythema of the cheeks in August, 1954. Progressive arthralgia of the ankles and knees began in October, 1954, and shortly thereafter the hands and wrists became involved to an incapacitating degree.

On admission there was noted erythematous, scaling lesions on the malar eminences and atrophy on the tips of the fingers. Considerable generalized joint pain, muscular weakness and atrophy, and a generalized lymphadenopathy were also present.

Laboratory study revealed a positive L. E. test (two-hour clot test and Haserick test). At that time a sister, age 22, who had had rheumatoid arthritis for two years also had a positive L. E. test. Other abnormal laboratory findings included trace of albuminuria, WBC 3700, ESR 60 mm. in an hour; VDRL test was positive undiluted only, and there was a negative Wasserman test.

Review of an old chart compiled in 1950, when the patient was hospitalized for a tonsillectomy, revealed a doubtful Kahn test, negative Wassermann test, WBC of 8150, and a total protein of 7.8 gm. % with albumin 4.2 and globulin 3.6 gm. %.

Since the original admission the patient has been treated intermittently with cortisone up to 200 mg. per day and Meticorten up to 90 mg. per day. Treatment with steroids had to be interrupted on two occasions because of psychotic episodes. These were apparently caused by the steroids rather than the lupus erythematosus and responded satisfactorily to the interruption of steroid therapy. He has had pneumonia seven times, three times while on steroids. Two of these bouts responded to antibiotics, while one responded to antibiotics with hydrocortisone. Pneumonia occurred twice while he was receiving steroids alone; one bout responding to an increase of steroids and the other to an increase of steroids along with penicillin and Chloromycetin.

At present the patient is receiving penicillin, Meticorten (5 mg. per day), and chloroquine (500 mg. per day).

Lupus Erythematosus, Subacute. Presented by Dr. Henry E. Michelson and Dr. Sheldon L. Mandel.

A 38-year-old man noted rough, scaly areas on the forehead and redness and flushing of the face, associated with fever, weakness, and easy fatigability in 1953. Muscle soreness and weakness, particularly in the arms and shoulders, and a decrease in manual dexterity coincided and produced a clinical picture similar to dermatomyositis. The condition has continued with exacerbations and incomplete remissions.

Some improvement followed the use of antimalarial compounds.

Violaceous, edematous, telangiectatic papules and disks without scaling are apparent on the face, neck, and over the knuckles. The muscles of the arms and shoulders are sensitive to touch but are not atrophic.

Studies revealed hemoglobin concentration of 13 gm. %, white blood cell count of 6000, with elevation of temperature to 99.2 to 99.8 F, especially after minimal exertion, and transient albuminuria. The L. E. clot test was negative.

The biopsy was acceptable for the diagnosis of lupus erythematosus.

Lupus Erythematosus in Extenso with Exacerbations. Presented by Dr. Henry E. Michelson and Dr. Sheldon L. Mandel.

A 29-year-old woman developed an eruption on the cheeks and face during her third pregnancy, in 1953. The cutaneous condition subsided after parturition but reappeared the following spring after exposure to sunlight. The eruption then involved larger areas on the exposed portions of the upper chest and the dorsae of the hands and arms. Persistent fever (99.4 to 100.0 F), easy fatigability, anemia, intermittent oppressive chest pain, weight loss, and susceptibility to upper respiratory infections were associated. The cutaneous lesions were extensive psoriasiform plaques which were often eroded, oozing, bloody, crusted, and at times pustular. Healed portions were atrophic and depigmented. The axillary lymph nodes and the spleen were enlarged.

Laboratory studies consistently showed anemia, hemoglobin 10 gm., white blood cell count 6000, sedimentation rate 40-50 mm. in an hour, and albumin-globulin ratio of 3.3 to 3.6 gm. %.

A biopsy specimen is presented.

In 1953, following the administration of Atabrine, the skin lesions healed and the patient's general health improved. One year later verrucous ulcerated areas on the arms persisted, despite antibiotic therapy, but improved following the administration of chloroquine. The drug was discontinued when she developed pigmented scalp hairs. She has been able to continue her household duties only with difficulty because of fatigue, weakness, frequent respiratory infections, and renewed activity of the painful cutaneous lesions. An exacerbation of the disease occurred in December, 1956, when she was in the first trimester of her fourth pregnancy. She received antimalarial therapy for brief periods and felt subjectively improved but continued to have active lesions on the face and forearms. A viable infant was born prematurely in April, 1957. Although there have been periods of relative improvement, this patient has been significantly handicapped and incapacitated since the onset of her illness.

Discussion

Dr. Louis Brunsting, Rochester, Minn.: I am much impressed by the group of patients with forms of lupus erythematosus and dermatomyositis. Many times the diagnosis cannot be established without prolonged observation. Sometimes the question of rheumatoid arthritis comes into the picture. Recently rheumatologists have called attention to the

finding of a positive L. E. test in cases of rheumatoid arthritis of long standing, especially in those in which the patient has been long-treated with steroids. I am more or less of the opinion that these may represent cases of lupus erythematosus after all. This situation is exemplified in one of the cases presented here, in which a close relative, a sister with presumably rheumatoid arthritis, was found to have a positive L. E. test. I would like to emphasize again that the management of these cases represents an individual problem and that the use of steroids is not the beginning and end of the treatment. In systemic lupus erythematosus, it is important, above all, to realize that the patient is brittle and that every effort should be made to conserve his natural resources and, furthermore, that the disease may be expected to manifest unexpected relapses in the face of intercurrent infection or excessive activity. Finally, as it appears here, it is impossible to make an estimate of prognosis or of the severity of the disease on the basis of the signs on the surface.

DR. STEPHEN ROTHMAN, Chicago: In the case of acute severe erythematosus and also in the case of lupus erythematosus in extenso, there is an interesting combination of the more stable chronic type of lesions with dissemination and systemic manifestations of lupus erythematodes.

DR. I. FISHER, Minneapolis: In the case of disseminated lupus erythematosus in the 28-year-old man, an interesting suggestion has been made concerning this patient. Within a relatively short period of time this man has had pneumonia on a number of occasions. He has had pneumonia twice in the past six months, had pneumonia in 1956, and had pneumonia on about four occasions in 1955. In spite of the fact that the patient does have an elevated globulin level, it was suggested that perhaps this globulin is sufficiently abnormal so that no immune bodies are produced by the patient. With that in mind, an attempted challenge by way of typhoid vaccine was suggested. The patient has been immunized twice with typhoid and paratyphoid in order to determine whether or not his blood titer does come up with such a challenge.

Lichen Sclerosus et Atrophicus of the Mouth. Presented by by Dr. HAROLD G. RAVITS. This case was reported in the A. M. A. ARCH. DERMAT., July, 1957.

Lichen Sclerosus et Atrophicus with Hemorrhagic Bullae. Presented by DR. HENRY E. MICHELSON and DR. SHELDON L. MANDEL.

Mycosis Fungoides. Presented by the Dermatology Department of the Duluth Clinic.

Mycosis Fungoides. Presented by the Minneapolis Veterans' Hospital.

Dermatomyositis. Presented by DR. IRVINE M. KARON.

Dermatomyositis (Periarteritis Nodosa?). Presented by DR. IRVINE M. KARON.

Sarcoidosis. Presented by the Staff of the University Hospital.

Abstracts from Current Literature

Clinical and Pathologic Findings in the Skin in Anaphylactoid Purpura (Allergic Anghitis). R. K. Winklemann, Proc. Staff Meet. Mayo Clin. 33:277-288 (May 28) 1958.

Hemorrhage is the basic and typical part of this syndrome. It is usually accompanied by an acute toxic onset. Histopathologically, there is acute necrotic involvement of vessel walls. Involvement of any system can occur. Often there are symetrical cutaneous lesions which are variable and include macular, papular, urticarial, or vesicular types. To illustrate the varied picture of the condition, five interesting cases are presented. Many are cases of dermatitis medicamentosa. Steroid therapy often is needed.

Norins, Chicago.

Experimental Production of the Acantholytic Phenomenon with Ammonium Hydrate. A. Tosti, Ann. ital. dermat. sif. 12:28-34 (Jan.-Feb.) 1957.

A marked acantholysis is caused by the application on the skin of a mild solution of ammonium hydroxide. The method may be useful for cytologic study of smears of normal and pathologic epidermis.

Ronchese, Providence, R. I.

The 17-Ketosteroids in Patients Treated with Sodium Hyposulphite. A. Grana and A. Longo, Ann. ital. dermat. e sif. 12:16-27 (Jan.-Feb.) 1957.

In atopic dermatitis and psoriasis, patients with low 17-ketosteroid values show a constant increase with the administration of sodium hyposulphite. In patients with high 17-ketosteroid values, a constant decrease was noted with the administration of the drug. No variations were noted in erythroderma and in leg ulcers.

Ronchese, Providence, R. I.

Acetylation in Psoriasis. I. Ciaccio and R. Pochy-Riano, Ann. ital. dermat. e sif. 12:3-15 (Jan.-Feb.) 1957.

In psoriatics there is a significant decrease in the acetylation rhythm, related to a decreased action of a coenzyme in the liver and in the skin, in close connection with an abnormal phosphorus metabolism.

Ronchese, Providence, R. I.

Contribution to Therapy and Pathogenesis of Abt-Letterer-Siwe Disease. I. Langer and G. Leonhardi, Arch. klin. u. exper. Dermat. 207:141-155, 1958.

The authors describe a case of Abt-Letterer-Siwe disease in a 1½-year-old child observed over a period of four years. The following clinical symptoms were found: hepatomegaly, lymphadenopathy, diabetes insipidus, dwarfism, hemorrhagic skin lesions, secondary anemia, and remittent fever. Histologic examination of a papule was interpreted as a later stage of ALS disease. Cortisone therapy combined with antibiotics given for two years kept the child alive. No complications developed during these two years. Subsequently, corticotropin, (ACTH) was administered for about six months. The child has been without treatment for one and one-half years, has developed satisfactorily, and only shows residual symptoms. The authors suppose that ALS disease is of endocrine origin. Possibly a quantitative and qualitative disturbance of the production of the adrenal cortex hormone exists, owing to dysfunction of the pituitary gland. Insufficiency of the adrenal cortex could cause reticular hypoplasia, which is checked by cortisone. The adrenal cortex recuperates, owing to ACTH therapy. After cessation of treatment, the pituitary gland again takes over the regulation of the disturbed metabolism.

Hollander, Springfield, Mass.

Extrarenal "Löhlein Focal Nephritis" of the Skin in Endocarditis. H. A. Gottron and W. Nikolowski, Arch. klin. u. exper. Dermat. 207:156-176, 1958.

In a 52-year-old woman with endocarditis lenta symmetrical erythematous, purpuric, and necrotic lesions of both cheeks, ears, and the extensor aspect of both upper arms developed. Histologically thrombotic and not embolic changes were found. The authors feel that their findings will help to clarify the pathogenesis of the so-called embolic focal nephritis of Löhlein.

Hollander, Springfield, Mass.

DEPOSITS OF HOMOGENEOUS SUBSTANCES (AMYLOIDOSIS, CALCINOSIS) IN OSLER'S DISEASE. H. A. GOTTRON and G. W. KORTING, Arch. klin. u. exper. Dermat. 207:177-201, 1958.

One case of Osler's disease with amyloidosis and two cases with calcinosis are described. PAS-positive tissue material was found in both amyloidosis and calcinosis.

HOLLANDER, Springfield, Mass.

PROBLEMS AND RESULTS OF X-RAY STUDY OF THE SKIN AND ITS DISEASES: PART I. METHOD AND RESULTS IN NORMAL SKIN. G. LEMKE, Arch. klin. u. exper. Dermat. 207:99-140, 1958.

A historic review of x-ray studies of soft parts without contrast media is presented. The authors give details of physicotechnical and biologic principles of the diagnosis of soft parts. Serial examinations were done on 200 persons of both sexes and all age groups. Various skin areas of the body were examined with a Siemens soft-ray therapy apparatus (Dermopan) at 10, 17, 20, 29, and 50 kv. A small, band-like shadow of 1 to 2 mm. width can be recognized regularly as the lateral border of the subcutis ("cutis line"). Differentiation of the cutis line for recognition of epidermis and cutis cannot yet be made. As far as the appendages of the skin are concerned, demonstration of nail and mammilla is possible, whereas, the individual hair, sebaceous, and sweat glands cannot be visualized. Demonstration of thick hair tufts is possible. Blood vessels and nerves within the cutis cannot yet be recognized without contrast media. The subcutaneous fatty tissue is sharply separated from the cutis line; it represents a physiologic contrast medium. There are two different elements recognizable in the subcutis. The first is a fine reticular net originating from the cutis line, resembling parallel palisades, then developing into coarse trabecles, and finally showing in the depth longitudinal fascia-like formations. The second element resembles the branches of a tree; it is broader and denser and represents blood vessels. Arteries and veins cannot be differentiated. Peripheral nerves in the subcutis have not been demonstrated so far with certainty. It is possible that they were previously evaluated as blood vessels. The subcutaneous muscle fascia is a very thin but distinct line, often demonstrable. Its recognition in severe edema of the subcutis is not possible. Muscle adjacent to the subcutis appears as a homogenous shadow. The x-ray picture of the skin does not allow any conclusions concerning sex, age, and topography. The only exception is senile atrophy of the skin.

HOLLANDER, Springfield, Mass.

ALOPECIA FOLLOWING TREATMENT WITH DEXTRAN SULPHATE AND OTHER ANTICOAGULANT DRUGS. G. R. TUDHOPE, H. COHEN, and R. W. MEIKLE, Brit. M. J. 1:1034 (May 3) 1958.

Alopecia occurred in 8 out of 15 patients treated with the anticoagulant drug dextran sulfate when the total dose was 90,000 or more units. The period of dextran sulfate therapy was less than one month in each case. Complete scalp alopecia occurred, and in several patients there was also pubic, axillary, and facial hair loss. The loss occurred between one and two months after treatment was discontinued. In each case there was a regrowth of hair. Transversely ridged nails were noted in three patients.

NORINS, Chicago.

THE RENAL LESION IN ANGIOKERATOMA CORPORIS DIFFUSUM. J. R. COLLEY, D. L. MILLER, M. S. R. HUTT, H. J. WALLACE, and H. E. DE WORSTENER, BRIT. Med. J. 1:1266 (May 31) 1958.

Two men in the same family suffered from angiokeratoma. Renal biopsies were performed on both men, and a characteristic vacuolation and distention of the cells of the glomerular tufts and distal tubules was found in each. The ability to concentrate urine was impaired in both. Identical lesions were found on reexamination of a kidney removed at autopsy from a female relative of these patients; she was the mother of one and the aunt of the other.

NORINS, Chicago.

STREPTOMYCIN DERMATITIS IN NURSES. H. WILSON, Brit. M. J. 1:1378-1382 (June 14) 1958.

Eighteen cases of dermatitis in nurses handling streptomycin were reported. There was an incidence of one case of dermatitis per 4000 injections. When the precautions of wearing gloves and masks during injections were carried out, the incidence was greatly reduced. There were positive patch tests in the reported cases. Six of the nurses were desensitized starting with doses of 2μg. and increasing with daily injections to 1 gm. of the streptomycin. All six were desensitized with a relapse in two of the cases after one year. After desensitization patch testing was negative and the nurses were able to handle the material. In each case there were reactions during the desensitization procedure.

NORINS, Chicago.

STATISTICS OF DERMATOSES DURING 1946-1956. R. CAVALIERI et al., Cronache dell'I. D. I. 12:205-255 (Nov.-Dec.) 1957.

The incidence of dermatoses in the Istituto Dermopatico dell'Immacolata in Rome in the decade 1946-1956 is tabulated. A sharp increase has been noted in alopecia areata, psoriasis, and varicose ulcers. A decrease in scabies, lupus vulgaris, trichophytosis of the scalp, and herpes simplex is evident.

RONCHESE, Providence, R. I.

TRICHOTILLOMANIA. R. CAVALIERI and G. C. SOAVI, Cronache dell'I. D. I. 2:86-93 (April) 1956.

This is a report on a case of trichotillomania in a 17-year-old girl feeling pleasure in certain areas (inversion of sense of pain) and pain in others. It started after watching haircutting in nuns and appealed to the patient as a renunciation of femininity to fight her developing sexuality. The pleasurable pulling of the hair substituted for the erotic pleasure. She was successfully treated by psychotherapy, and the procedure is described at length.

RONCHESE, Providence, R. I.

CHRONIC DISCOID LUPUS ERYTHEMATOSUS TREATED WITH INTRADERMAL CHLOROQUINE. A. LEONI, Dermatologia 8:33-34 (Feb.) 1957.

In six cases the clinical cure was complete, in three partial, and in three there was no result. Lesions injected with distilled water and untreated lesions located far from the treated ones improved considerably.

RONCHESE, Providence, R. I.

PORPHYRIA CUTANEA TARDA. G. C. FUGA, Dermatologia 8:197 (July); 8:231 and 233 (Oct.) 1957.

In six cases of porphyria cutanea tarda the chromic diffusion with physiologic solution, hyaluronidase, and hydrocortisone showed no variations from normal subjects. The ungual capillaries were found larger than normal and increased in number. Petechiae formed on pressure applied with Riva-Rocci sphygmomanometer.

RONCHESE, Providence, R. I.

DIFFUSE ALOPECIA IN WOMEN. M. SANNINO and D. MONTEMURRI, Dermatologia 8:193-197 (July) 1957.

An increase in the incidence of diffuse alopecia in women was noted in recent years. In 45 cases, among the 95 investigated, exaggerated reflexes, anxiety, tension, and psychic conflicts were found. The disorder could be a consequence of the present-day rhythm of life.

RONCHESE, Providence, R. I.

SEBUM TEST AFTER ROENTGENOTHERAPY. A. R. COFANO, Dermatologia 8:200-206 (July) 1957.

The osmic acid sebum test showed a gradual diminution of the chromatic intensity from the first to the seventh day of observation, either with one massive dose or with several fractional ones.

RONCHESE, Providence, R. I.

EOSINOPHILE GRANULOMA OF VULVA AND BONE AND DIABETES INSIPIDUS. A. RIBUFFO, Dermatologia 8:165-174 (June) 1957.

A discussion on the possible relationship between eosinophilic granuloma of the skin and eosinophilic granuloma of the bone.

RONCHESE, Providence, R. I.

THE HISTOLOGY OF CONTACT DERMATITIS. L. BUSINCO, W. GRANELLI, A. GAFFI, and G. CENTANNI, Folia allergologica 4:479-485 (Nov.-Dec.) 1957; Internat. Arch. Allergy 2:44-60, 1957.

The main changes are in the capillaries, showing increased permeability, serum imbibition, and edema of surrounding tissue. The capillaries may also show an increase in peripheral histiocytes.

RONCHESE, Providence, R. I.

PORPHYRIURIA AND DIURESIS IN CONGENITAL PORPHYRIA. F. OTTOLENGHI-LODIGIANI, Gior. ital. dermat. e sif. 98:601-610 (Nov.-Dec.) 1957.

A case of congenital porphyria was studied for 75 days during which the patient had five periods of aggravation of symptoms. During these periods the porphyrinuria increased and the

diuresis decreased, then returned to normal. The variations are attributed to porphyrin metabolism and not to the function of the kidneys.

RONCHESE, Providence, R. I.

THE DISTRIBUTION OF ALKALINE PHOSPHATASE IN THE SKIN. G. FARRIS, Gior. ital. dermat. e sif. 98:612-634 (Nov.-Dec.) 1957.

Enzymatic localizations of alkaline phosphatase, demonstrated with the Gomori method in man and in guinea pigs, are discussed. The paper is profusely illustrated.

RONCHESE, Providence, R. I.

MELANINOGENESIS AND ITS RELATIONS WITH ANALOGOUS BIOCHEMICAL PROCESSES. S. SACCHI, Gior. ital. dermat. e sif. 98:635-653 (Nov.-Dec.) 1957.

A discussion about the probability of comparison between melaninogenesis, enteraminogenesis, adrenalinogenesis, and quinonic tanning and the possible multiple origin of melanin.

RONCHESE, Providence, R. I.

SUCCINODEHYDROGENASIS OF THE SKIN. M. BINAZZI, Gior. ital. dermat. e sif. 98:509-525 (Sept.-Oct.) 1957.

The study was done on skin of various areas, in various ages, in sun-damaged skin, in diabetes, and in many other miscellaneous dermatoses. Higher succinodehydrogenasis activity was found in conditions of intense metabolic activity. It was found to be reduced in pemphigus and particularly high in dermatitis herpetiformis.

RONCHESE, Providence, R. I.

CONGENITAL ECTODERMAL DYSPLASIA. L. DATOVO and L. LEVI, Gior. ital. dermat. e sif. 98:526-535 (Sept.-Oct.) 1957.

A case of anhydrosis from obliteration of ducts and pores while the glands were present and functioning is presented.

RONCHESE, Providence, R. I.

THE EFFECT OF TOPICAL APPLICATIONS OF COLCHICINE ON NORMAL SKIN. S. D. RANDAZZO, Minerva dermat. 32:305-311 (Aug.) 1957.

The use of N-desacetylmethylcolchicine in epithelioma, precancerous dermatoses, and leg ulcers has been previously investigated (*Dermatologia*, p. 167, 1955; pp. 33, 138, 297, 1956). In this study colchicine was applied on normal skin in 22 patients affected by various dermatoses. The effect is similar to the one obtained by carbon dioxide snow and by ultraviolet rays. The chemical causes a conspicuous dermoepidermic separation.

RONCHESE, Providence, R. I.

THE SECRETION OF SEBUM DURING AND AFTER PREGNANCY. M. DEPAOLI, Minerva dermat. 32:89-93 (March) 1957.

The osmic acid test was done in 15 women toward the end of pregnancy and a few days after pregnancy. The quantity of sebum was higher during pregnancy.

RONCHESE, Providence, R. I.

THE EFFECT OF VITAMIN C ON THE COLOR OF GRAFTED SKIN. M. VISETTI and F. FERRERO, Minerva dermat. 32:457-459 (Dec.) 1957.

High doses of vitamin C intravenously inhibit the tyrosine-tyrosinase-melanin reaction, with consequent hypopigmentation of the grafted skin.

RONCHESE, Providence, R. I.

ELECTROENCEPHALOGRAPHY AND ELECTRODERMATOGRAPHY IN PSORIASIS. A. GUIDA and C. SABATINI, Minerva dermat. 32:101-105 (April) 1957.

In 15 psoriatics the bioelectrical variations from the normal appeared in part similar to those found in psychoneurosis and anxiety.

RONCHESE, Providence, R. I.

REACTION TO POTASSIUM IODINE IN NORMAL SUBJECTS, IN DERMATITIS HERPETIFORMIS, AND IN PEMPHIGUS. V. MUSUMECI, Minerva dermat. 32:119-124 (April) 1957.

Potassium iodide was given in large doses internally and applied topically. The dermoepidermic separation was conspicuous and was obtained with low concentrations in pemphigus

and dermatitis herpetiformis. The same low concentrations produced no dermoepidermal changes in normal skin.

RONCHESE, Providence, R. I.

PHYSIOPATHOLOGY OF VESICLES AND BULLAE. V. MUSUMECI, Minerva dermat. *32*:270-277 (July) 1957; *32*:395-400 and 400-405 (Nov.) 1957; *33*:44-48 (Feb.) 1958.

Human skin, immediately after excision, was treated with cisteine, cistine, glutatione, and thioglycolic acid.

Trypsin, papain, and lipase were injected in normal subjects and into skin immediately after its excision. In the excised skin the effect was much more severe, the epidermis often becoming necrotic. No trace of the enzymes was found in the fluid of the bullae.

In normal subjects and in cases of pemphigus and of dermatitis herpetiformis Musumeci injected diastase, saliva, and hyaluronidase. No effects were noted in normal and in diseased skin. Dermoepidermic separation and disappearance of the mucopolysaccharide component of the basal layer was noted in the excised skin.

RONCHESE, Providence, R. I.

PALMO-PLANTAR KERATODERMIA. G. MONTILLI, M. PISANI, and C. SERRA, Minerva dermat. *32*:33-49 (Feb.) 1958.

In four cases variations of the electrolytic balance was found, with a lowered K/Ca ratio. In one case the encephalogram revealed signs of involvement of the temporocentral basal structures. In three cases signs were found of localized or diffused immaturity and of electrical lability after photostimulation. Changes of the myogenous type were found in all four cases on electromyographical examination.

RONCHESE, Providence, R. I.

THE ALKALINE PHOSPHATASE AFTER ROENTGEN EXPOSURE. G. FARRIS and L. OLIVA, Minerva dermat. *32*:365-378 (Oct.) 1957.

Human and guinea pig skin was exposed to doses varying from 500 to 10,000 r. The skin, examined with the Gomori method, revealed more positivity in guinea pigs below the basal layer. In human skin no difference was found in the epidermis but marked increase was found in the dermis.

RONCHESE, Providence, R. I.

STIMULATION OF THE DIENCEPHALON-PITUITARY REGION IN MALIGNANT ALOPECIA AREATA. A. MIDANA and R. LEONE, Minerva dermat. *32*:355-360 (Oct.) 1957.

The stimulation was done by x-rays and by administration of soluble lipid diencephalic extract. More rapid effect was obtained with the diencephalic extract.

RONCHESE, Providence, R. I.

BOWEN'S DISEASE. F. ORMEA and P. RESSA, Minerva dermat. *32*:311-315 (Aug.) 1957.

This is a case of squamous-cell epithelioma of the glans penis, showing, as an unusual feature, sinuses filled with whitish material containing cancer cells.

RONCHESE, Providence, R. I.

DERMATO-FIBROMA OF DARIER AND FERRAND. G. MARSON, Minerva dermat. *32*:49-56 (Feb.) 1957.

A report of three cases is presented. The author is against the term fibrosarcoma because the disorder is clinically and histologically different from the various kinds of sarcoma. He considers it as a peculiar fibroma.

RONCHESE, Providence, R. I.

Books

Compendio di sessuologia. By G. Santori. Price, Lire 3000. Pp. 440, with 19 illustrations. Orizzonte Medico, Via della Conciliazione 4 D, Rome, 1958.

Sexology, venereology, syphilology, and dermatology are closely related subjects in European curricula. Santori, a distinguished dermatologist of Rome, gives in this handbook a clear and exhaustive view of what is known today on sexology.

Tratamento da cromoblastomicose pelo calciferol. By Clovis Bopp, M.D. Price, not given. Pp. 178, with 117 illustrations. Livraria de Globo, Of. Graf. da Livraria do Globo, Porto Alegre, Brazil.

Chromoblastomycosis, a common deep mycosis in Latin America, is notoriously resistant to therapy. In this monograph the author presents his experiences in the treatment of chromoblastomycosis with calciferol.

He acknowledges that calciferol has been previously recommended in the treatment of chromoblastomycosis by Castro Palomino and Armenteros in Cuba, Latapí in Mexico, and Bonilla in Costa Rica. His series of 20 carefully studied cases is the largest one reported, and allows comparison of the effects of the medication administered on different schedules. First, 600 units of calciferol were given daily. The lesions improved in four to six weeks, but signs of toxicity developed. Later, the medication was administered every second day; the most satisfactory results were obtained with weekly doses of calciferol, with a total of 15 to 25 doses. In all three schedules, the patients received 1 to 3 gm. of potassium or sodium iodide and routine local treatment (compresses, Unna's boot, etc.). The average time for cure varied between three and six months. Often cases that were apparently clinically cured presented tuberculoid structures containing fungus which represented an eventual focus of relapse.

The author concludes that calciferol associated with iodides and occlusive dressings represents the most effective, rapid, and consistent treatment of chromoblastomycosis.

This well-written monograph is excellently illustrated with many clinical and histopathological photographs. It has a complete bibliography and a summary in English. It is recommended to all those interested in tropical dermatology and mycology.

Blastomicose Sul-Americana. Estudo das lesãoes dentárias e paradentárias sob o ponto de vista clínico e histopatológico. By José Bonifácio Fonseca. Price, not given. Pp. 182, with 20 plates. Politipo Ltda., Rua Asdrubal do Nascimento 114, São Paulo, 1957.

This monograph presents a complete study on the dental and periodontal changes caused by Paracoccidiodes brasiliensis. After a brief review of the previous knowledge on the subject, the author adds many valuable original contributions through a methodical investigation of 25 cases. Each case was carefully studied clinically, radiologically, and histologically, utilizing the most modern laboratory techniques. The author stresses the role of the oral lesions as initial symptoms of South American blastomycosis, as this occurred in 18 out of 25 cases. He discusses the possible mechanism of introduction of P. brasilienses through certain habits of rural workers, like picking their teeth with twigs, chewing stalks and leaves, etc. Periodontal symptoms simulating "pyorrhea," pain and dental mobility are common. The topographic distribution and their tendency toward localization or dissemination of the disease was carefully evaluated. Besides the gum, the more frequently affected regions were the lips, palate, floor of the mouth, and the tongue.

The radiological findings more often observed were generalized, alveolar bone reabsorption of the horizontal type, sometimes coexisting with vertical reabsorption. The author stresses the fact that in many cases, clinically and radiologically suggestive of simple periodontitis, P. brasiliensis was found in histological examination.

This monograph clearly demonstrates that a great deal may be gained by careful investigation, clinical, radiological, and histological, of the teeth and periodontal tissue. It emphasizes the importance of a close cooperation between the dermatologist and the dentist in the study of South American blastomycosis.

Excellent illustrations of the clinical, radiological, and histological aspects of each case are presented. There is an extensive bibliography. This monograph is another example of the excellent investigations recently published in Latin America. It is recommended to all dermatologists and dentists interested in tropical diseases.

Year Book of Dermatology and Syphilology (1957-1958 Year Book Series). By Rudolf L. Baer, M.D., and Victor H. Witten, M.D. Price, $8.00. Pp. 492. The Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

The featured subject in this edition concludes the discussion begun in last year's edition of allergic eczematous contact dermatitis, and considers test procedures, prophylaxis, and treatment, including treatment with corticosteroids and corticotropin (ACTH). Included also are suggestions for the making of a routine screening tray and a long list of materials with concentrations and vehicles to be used in patch-testing. The remainder of the book adheres to the format of previous editions—careful selection of articles for abstracting with pertinent, crisp editorial comments. The division of material is practical, with sections devoted to treatment of various kinds, eczematous and drug eruptions, cancers, infections, miscellaneous dermatoses, and a section of 75 pages devoted to other investigative studies dealing chiefly with fundamentals of pathophysiology, biochemistry, pathology, pharmacology, etc.

Baer and Witten have again placed us in their debt with this edition of the Year Book. Because of their industry, it is possible for the rest of us to continue to benefit from a valuable postgraduate course in a most leisurely and pleasant manner. There will be many occasions when the dermatologist will be glad to have this book at hand.

Clinical Enzymology. Edited by Gustav J. Martin, Sc.D. Price, $6.00. Pp. 241. Little, Brown & Company, 34 Beacon St., Boston 6, 1958.

This volume heralds the approach of a new type of medicinal chemistry—one that in the future will "startle the world of classical biology." All phases of clinical enzymology are given consideration in this book; chemistry, biochemistry, much clinical data, laboratory diagnostics, therapeutic effects and even a look into the future with regard to the parenteral use of enzymes in disease. Topical use is not reviewed.

The idea of "biological relativity" is developed in a manner which is similar to Einstein's theory of relativity in the field of physics. According to this, no enzyme has only one function, its functions depend rather on its environment and are relative to the substrate that presents itself. No ion or molecule can be added to a biological system without modifying the behavior of every component of the system. Then follow chapters on the biochemistry of enzymes, the parenteral use of enzymes in various diseases, especially where extravascular fluid accumulation is associated with stasis, thrombophlebitis, ulcers, cellulitis, trauma, refractory wounds, etc. Enzymes as diagnostic aids are then considered as for instance, serum amplase in pancreatic disease, lysozyme determinations in peptic ulcer, hyaluronidase as a spreading factor test in rheumatic fever, increased uropepsinogen in urine in peptic ulcer and carcinoma of the stomach, acid and alkaline phosphatase determination in various diseases, etc. Much in the book is highly theoretical, some of it esoteric, but withal, it is an important contribution in that there are extensive references to pertinent literature, consideration is given to views that oppose those of the authors, that which is known is reviewed, that which is hoped for is delineated. It affords, in one volume, a view of what is going on in the field.

Dermatological and Serological Aspects of Allergy: Transactions of the Collegium Internationale Allergologicum; Third Symposium in London, March 25, 1957. Edited by R. R. A. Coombs, D. Harley, and P. Kallos. Price, not given. Pp. 236. S. Karger A. G., Arnold Böcklinstrasse 25, Basel, 1958.

This volume contains several interestingly written papers. R. L. Mayer, the allergist, and Werner Jadassohn debate the old question of contact dermatitis versus atopic dermatitis. Mayer, representing the unitarian school, considers them to be immunologically the same; "whether an allergenic agent produces contact or atopic dermatitis depends upon endogenous or exogenous factors." Jadassohn, of the dualist school, states, "the differences between atopic dermatitis and contact eczema are great," pointing to the generally recognized differences in passive transfer, hereditary tendencies, skin-test reactions, clinical pictures, response to treatment, etc. Incidentally, the two authors consider both conditions to be of allergic origin.

The gel-precipitation method as a tool in allergy is discussed by several authors. In a discussion of nickel sensitivity in women, Calnan points out several separate clinical manifestations of the condition: the primary lesion in the area of contact; secondary lesions of the sensitization type occurring in specific symmetrical areas as the cubitals, eyelids, sides of the neck, and inner thighs, and, thirdly, patches of associated nonrelated dermatitis on other areas. Keratin has a strong affinity for nickel.

This 235-page collection of papers is well worth reading. All but one of the contributors are European, and all but two of the articles are in English. The two French articles have English summaries.

Living with Your Allergy. By Samuel M. Feinberg, M.D. Samuel M. Feinberg, M.D. Price, $1.25. Pp. 190. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia, 1958.

It seems that there are about 17,000,000 persons in the United States who have "allergic ailments," and the proportion of these who understand their ailment is small. The author, an authority in allergy, has written this pocket-sized paper-back in simple language and informatively so that the victim may better understand allergy and learn to live with his ailment. The case-example, first-name-familiarity approach is used effectively; the information dispensed is, on the whole, rather sketchy, but it is probably adequate to alert the type of person who would neglect his ailments. The chapter headings, designed to attract attention, as for instance, "It's an Ill Wind," are effective, but the one covering drug eruptions might have been titled better than "Doctor-Made Allergies." By and large, however, the material is presented adequately and it is easy to read.

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References: (1) Zimmerman, M. C.: Clin. Med. *5*:305, 1958. (2) Becker, R. M.: New England J. Med. *254*:952, 1956. (3) Chen, J. Y. P.; Bard, J. W., and Balsito, A. A., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 321. (4) Minno, A. M., and Davis, G. M.: J.A.M.A. *165*:222 (Sept. 21), 1957. (5) Zimmerman, M. C., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 312. (6) Becker, R. M.: Ann. Int. Med. *48*:1228, 1958. (7) Becker, R. M., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 310. (8) Davis, G. M.: Discussion, Antibiotics Symposium, Washington, D. C., October 3, 1957. (9) Zimmerman, M. C.: J.A.M.A. *167*:1807 (Aug. 9), 1958.

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1. Saperstein, R. B.: Presented at 107th annual meeting of American Medical Assn., San Francisco, Calif., June 23-27, 1958.

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Summary of Clinical Effects of Triamcinolone on Dermatoses in Fifty-one Patients.[1]

TYPE OF LESION	HELPED, NO.	NOT HELPED, NO.
Chronic eczematous eruptions, including atopy	14	5
Localized neurodermatitis	4	2
Contact dermatitis	6	6
Seborrheic dermatitis	9	0
Alopecia areata	4	1

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with a low incidence of gastric disturbance [1,2,5,8]
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with no potassium loss [4, 8]
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with no adverse effect on blood pressure [1,2,4,5,7]
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1. Shelley, W.B.; Harun, J.S., and Pillsbury, D.M.: J.A.M.A. *167*:959 (June 21) 1958. 2. Sherwood, H., and Cooke, R.A.: J. Allergy *28*:97 (March) 1957. 3. Boland, E.W.: Geriatrics *13*:190 (March) 1958. 4. Hellman, L., and others: A.M.A. J. Dis. Child. *94*:437 (Oct.) 1957. 5. Hartung, E.F.: J.A.M.A. *167*:973 (June 21) 1958. 6. Feinberg, S.M.; Feinberg, A.R., and Fisherman, E.W.: J.A.M.A. *167*:58 (May 3) 1958. 7. Friedlaender, S., and Friedlaender, A.S.: Antibiotic Med. & Clin. Ther. *5*:315 (May) 1958. 8. Dubois, E.L.: J.A.M.A. *167*:1590 (July 26) 1958.

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With DECADRON, investigators note "a decided intensification of the anti-inflammatory activity"[3] and antirheumatic potency.[4] Clinically, this was manifested by a **higher degree of improvement** in many patients previously treated with prednisteroids,[3] and by **achievement of satisfactory control in an impressive number of recalcitrant cases.**[3,4]

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More patients can be treated **more effectively** with DECADRON. Its higher anti-inflammatory potency frequently brings relief to cases resistant to other steroids. Relative freedom from diabetogenic effect in therapeutic dosage permits treatment of certain diabetics without an increase in insulin requirements. Minimal incidence of hypertension and of sodium and fluid retention allows effective therapy of many patients with cardiovascular disorders. And a healthy sense of well-being, reported by nearly all patients on DECADRON, assures excellent patient cooperation.

References:
1. Boland, E. W.: California Med. 88:417 (June) 1958. 2. Bunim, J. J., et al.: Arthr. & Rheum. 1:313 (Aug.) 1958 3. Boland, E. W., and Headley, N. E.: Paper read before the Am. Rheum. Assoc., June 21, 1958, San Francisco, Calif. 4. Bunim, J. J., et al.: Paper read before the Am. Rheum. Assoc., June 21, 1958, San Francisco, Calif.

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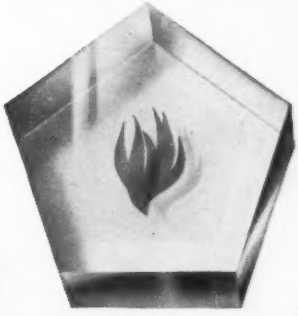
SUPPLIED:
As 0.75 mg. scored pentagon-shaped tablets; also as 0.5 mg. tablets, to provide maximal individualized flexibility of dosage adjustment.



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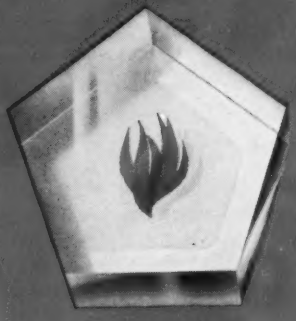

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1. Pflag, S.C. and Zopf, L.C.; Hydrophilic Forms of Tars, *U. S. Armed Forces M. J.* 2:1177-1181 (Aug.) 1951.

2. Carney, R.G. and Zopf, L.C.; An Improved Coal Tar Ointment Using a Surfactant, *Arch. of Dermat.* 72:266-271 (Sept.) 1955.

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*Miller, J. M.; Godfrey, G. C.; Ginsberg, M., and Papastrat, C. J., in Surgical Service, V. A. Hospital, Fort Howard, Maryland: Postgrad. Med. *22*:609, 1957.

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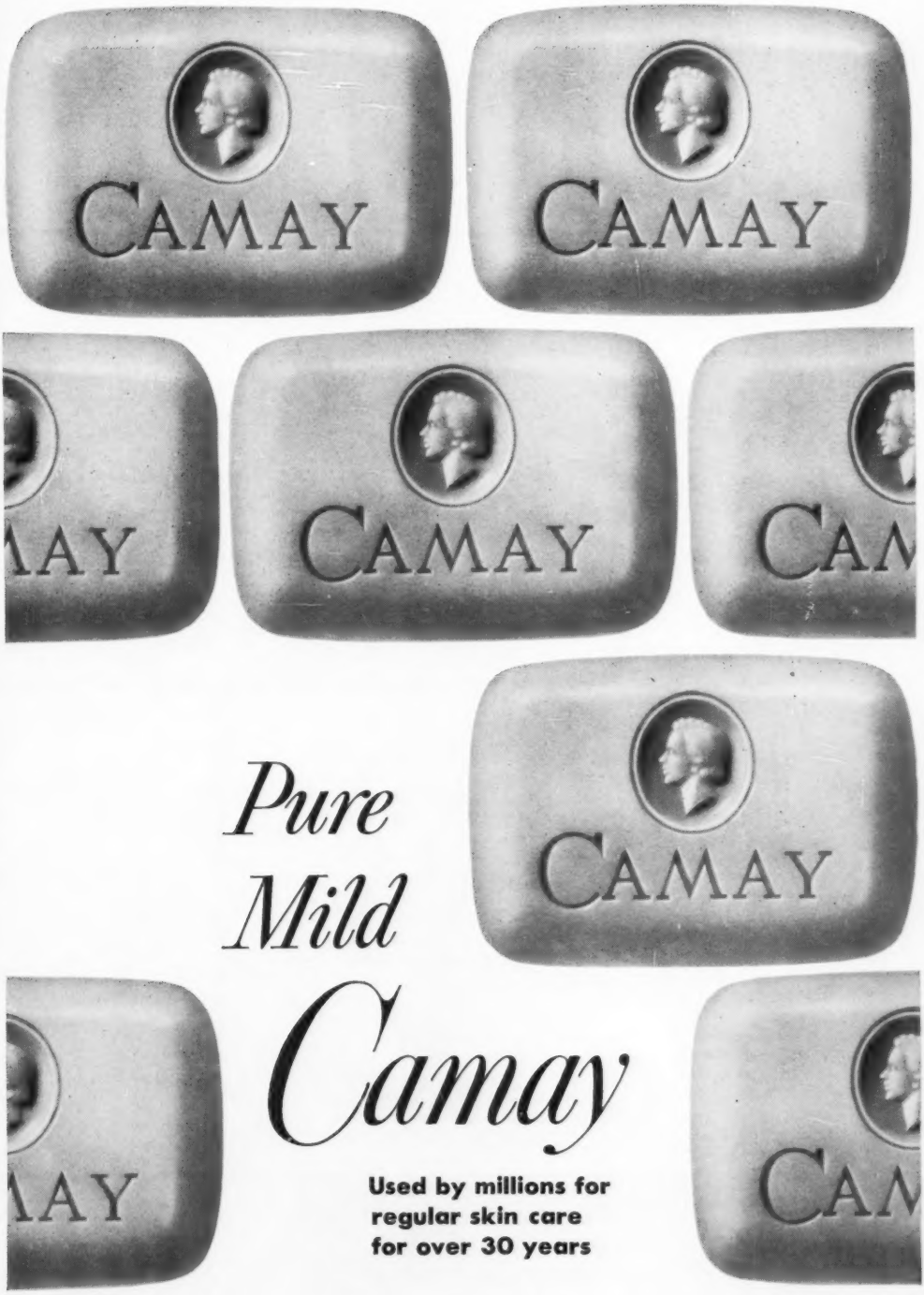

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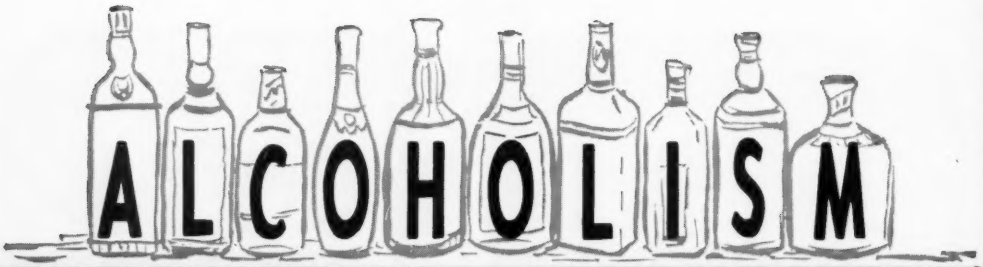

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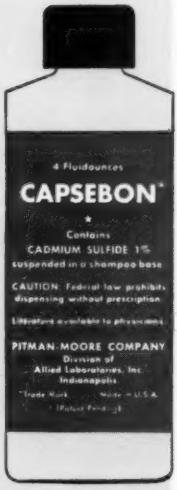

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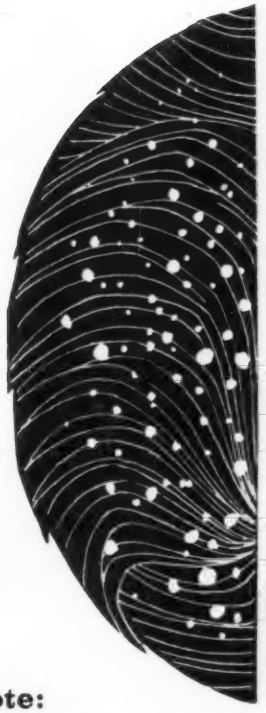

note:

If you are treating a patient for acne vulgaris may we suggest that you prescribe Capsebon to clear up associated seborrhea oleosa capitis.[4]

references: 1. Kirby, W. L.: Preliminary and short report. Cadmium sulfide suspension in seborrhea capitis. J. Invest. Dermat. *29*:159 (Sept.) 1957. 2. Stough, D. B.; Lewis, R. A.; Farmer, B. L.; Osment, L. S., and Noojin, R. O.: New beneficial agents in the treatment of acne vulgaris and seborrheic dermatitis. Postgraduate Medicine. In press. 3. Mullins, J. F., and Barnett, J. R.: Cadmium shampoo treatment of seborrheic dermatitis. Texas J. Med. *53*:640 (Aug.) 1957. 4. Reports in the Pitman-Moore Research Files, to be published.

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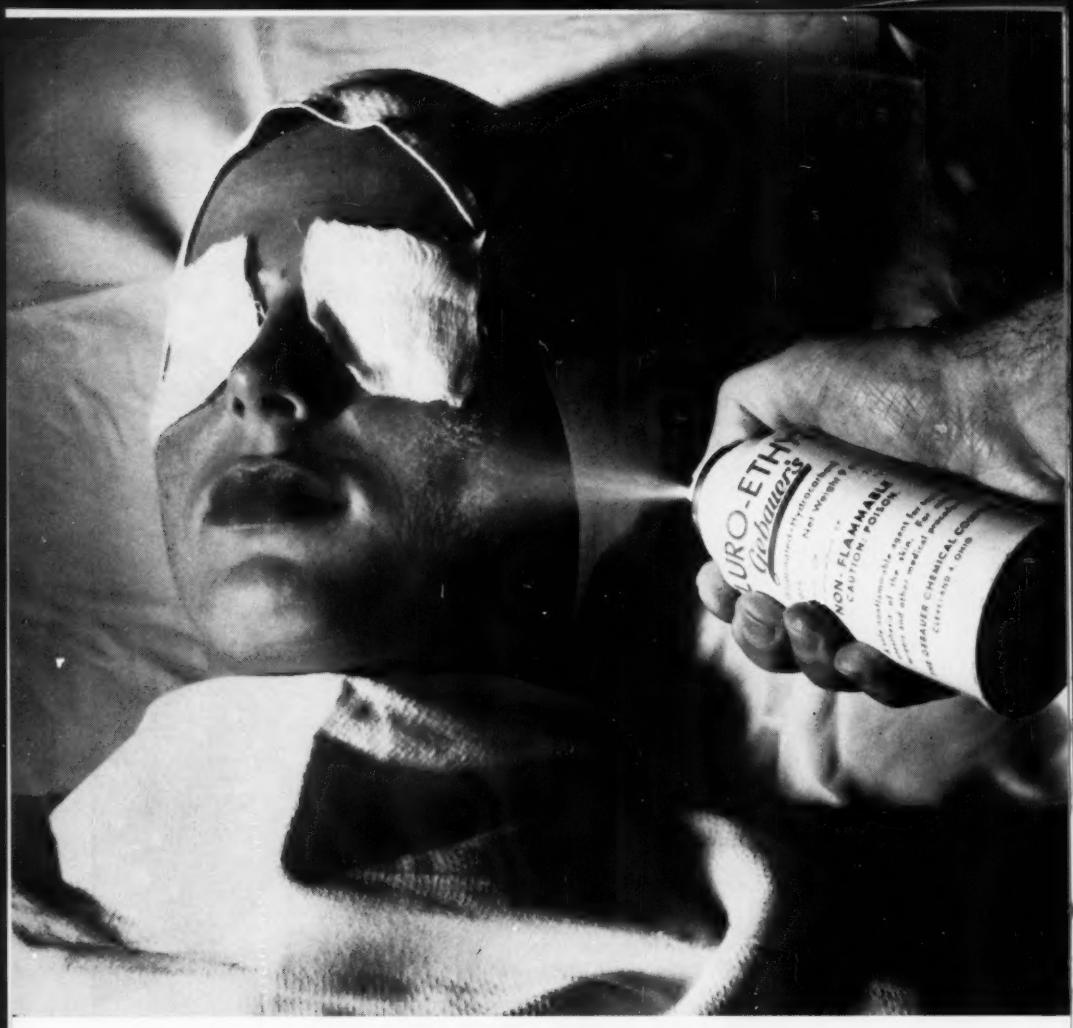

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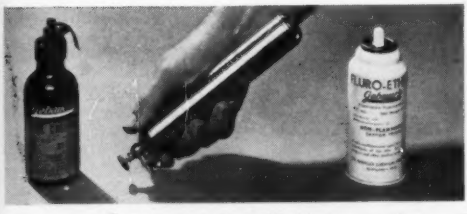

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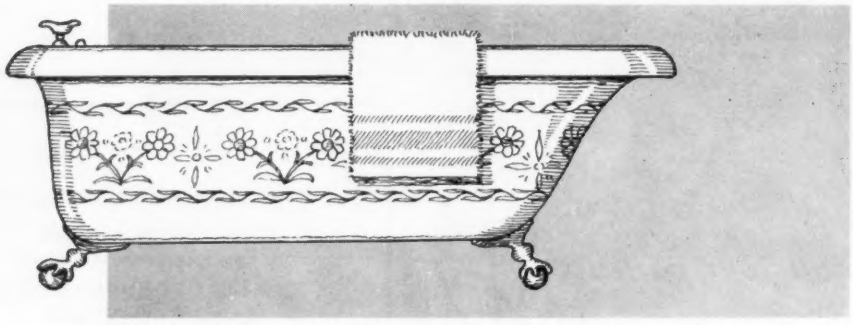

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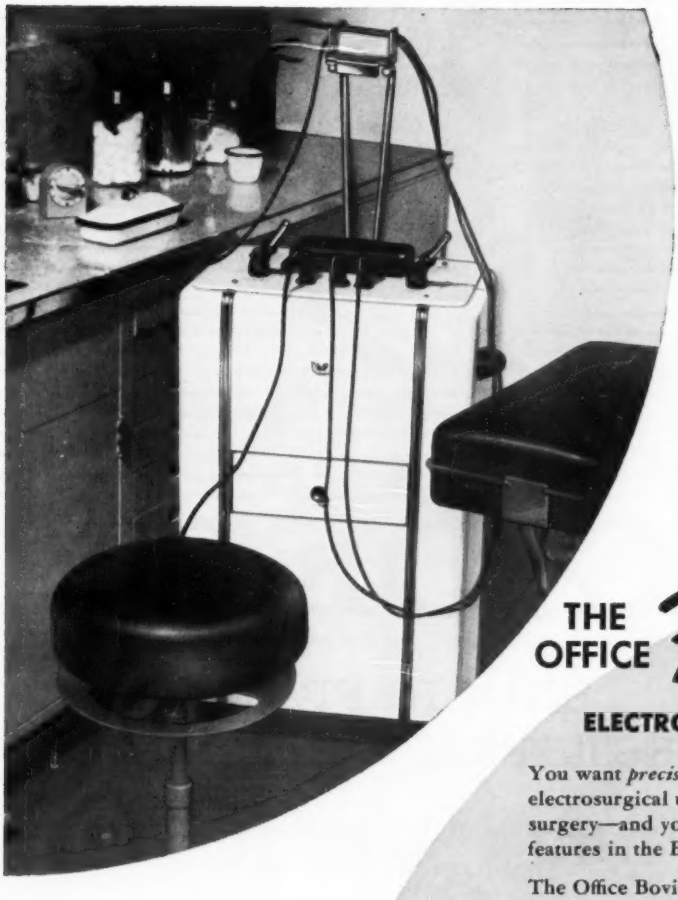

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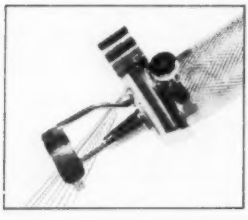

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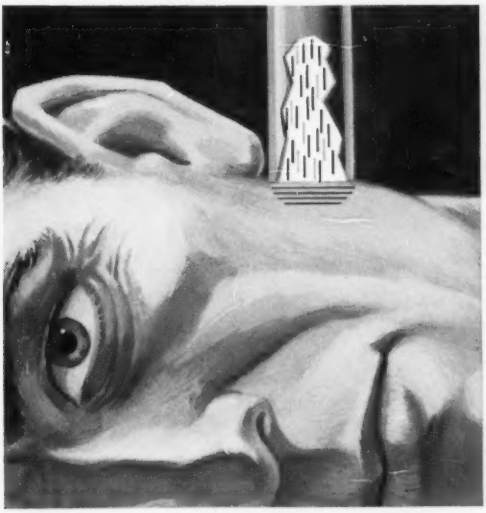

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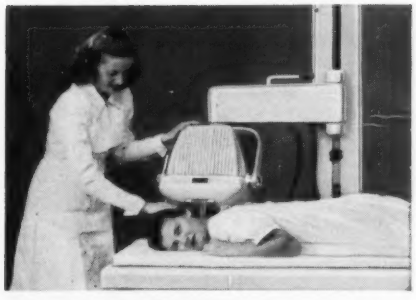

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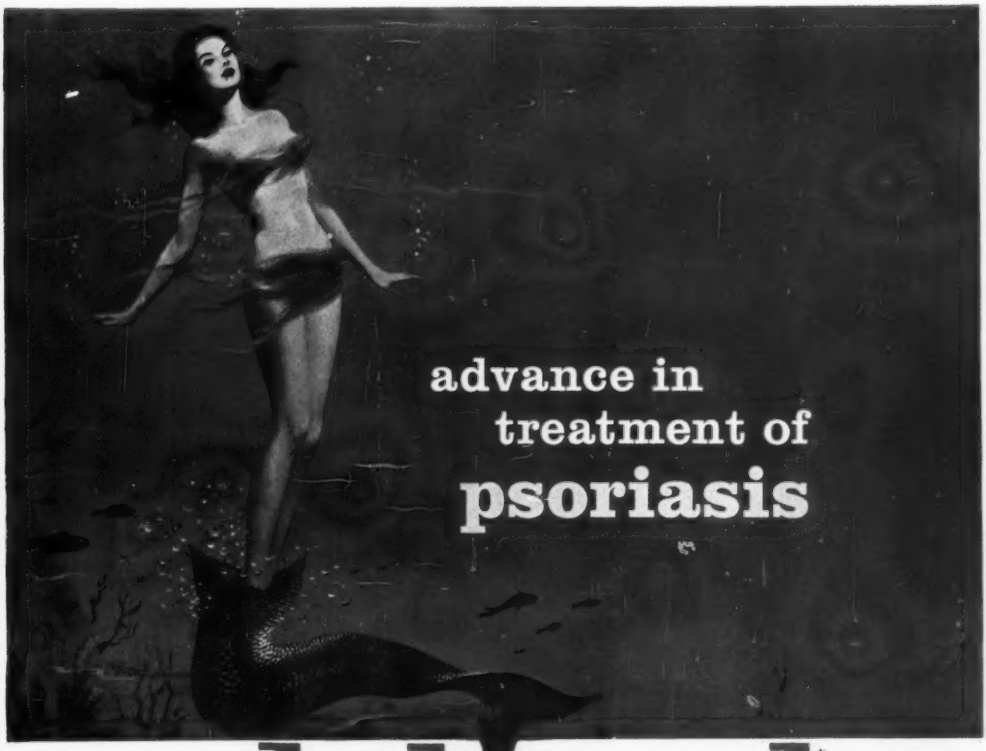

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(1) Flesch, P.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). (2) Bleiberg, J., and Saltzman, J. A.: Clin. Med. *5*:485 (Apr.) 1958. (3) Bleiberg, J.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). (4) Clyman, S. G.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). *Trademark

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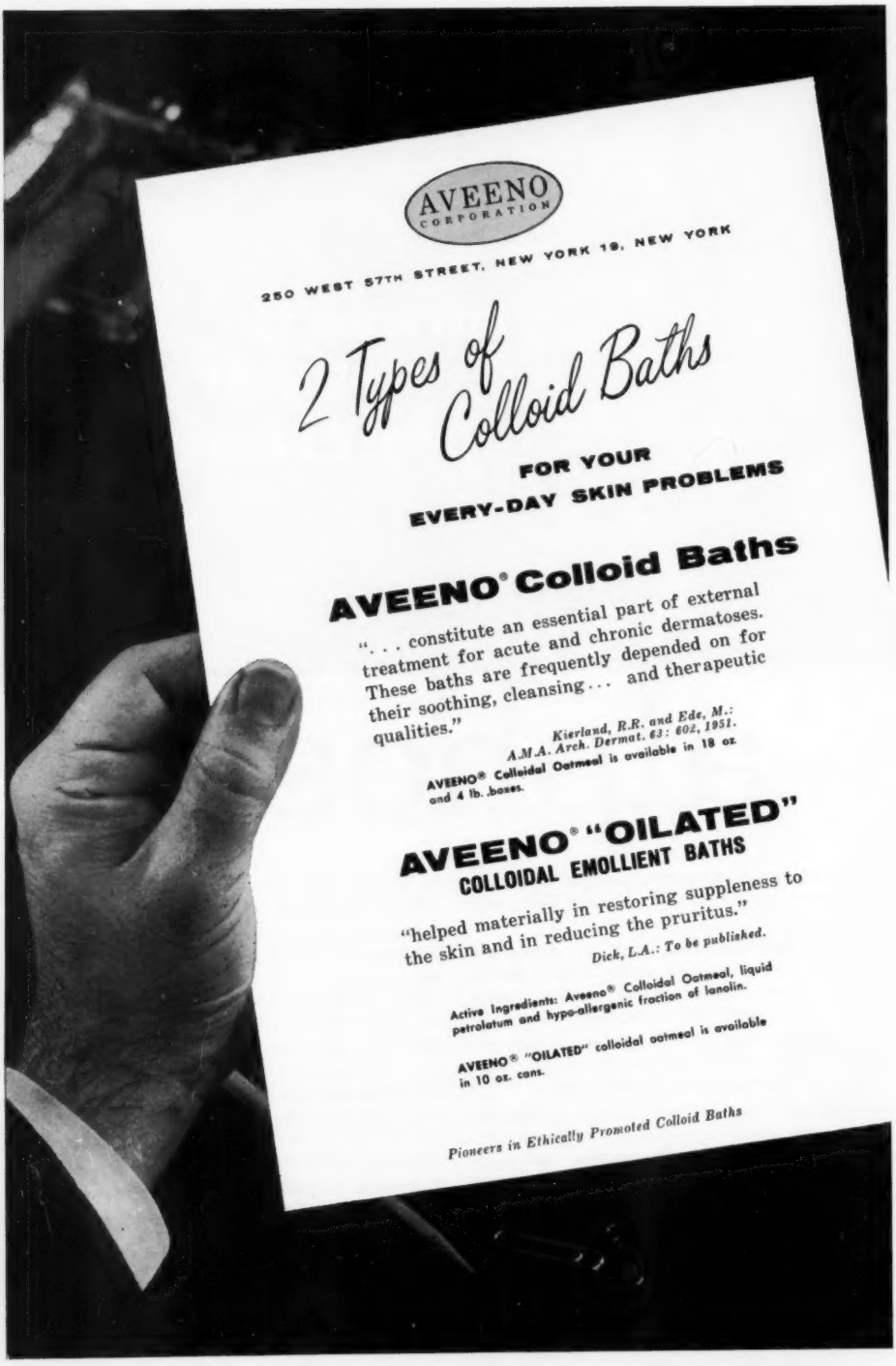
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REFERENCE:
Knox, J. M., Everett, M. A., and Curtis, A. C.: New Uses For Surface-Active Agents. A.M.A. Arch. Derm. 74:699-706 (Dec. 1956)

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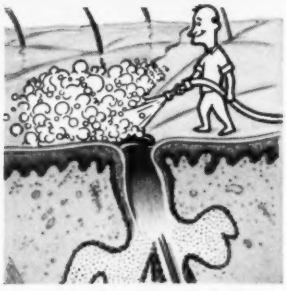

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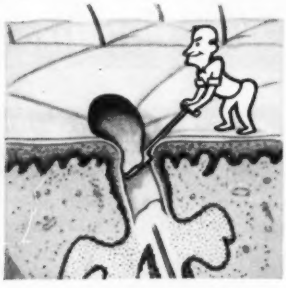
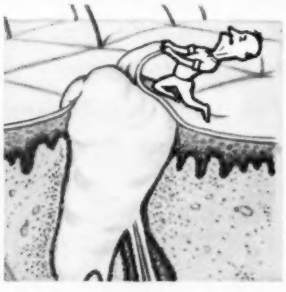


◂ Penetrate and soften comedones, unblocking the pores and facilitating removal of sebum plugs.



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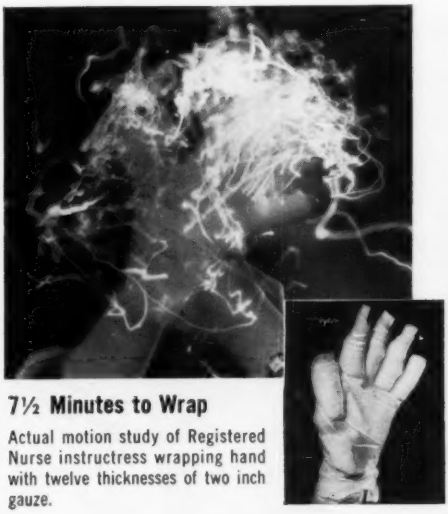

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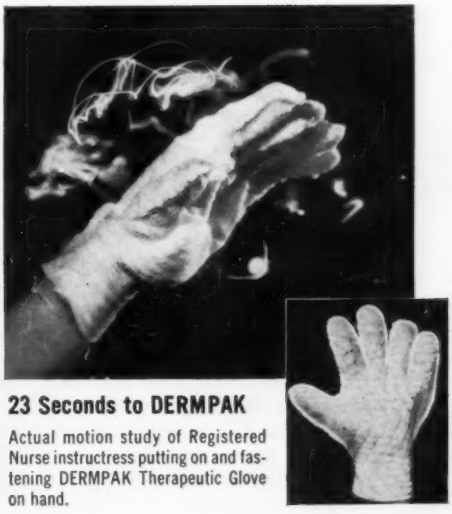
Actual motion study of Registered Nurse instructress wrapping hand with twelve thicknesses of two inch gauze.



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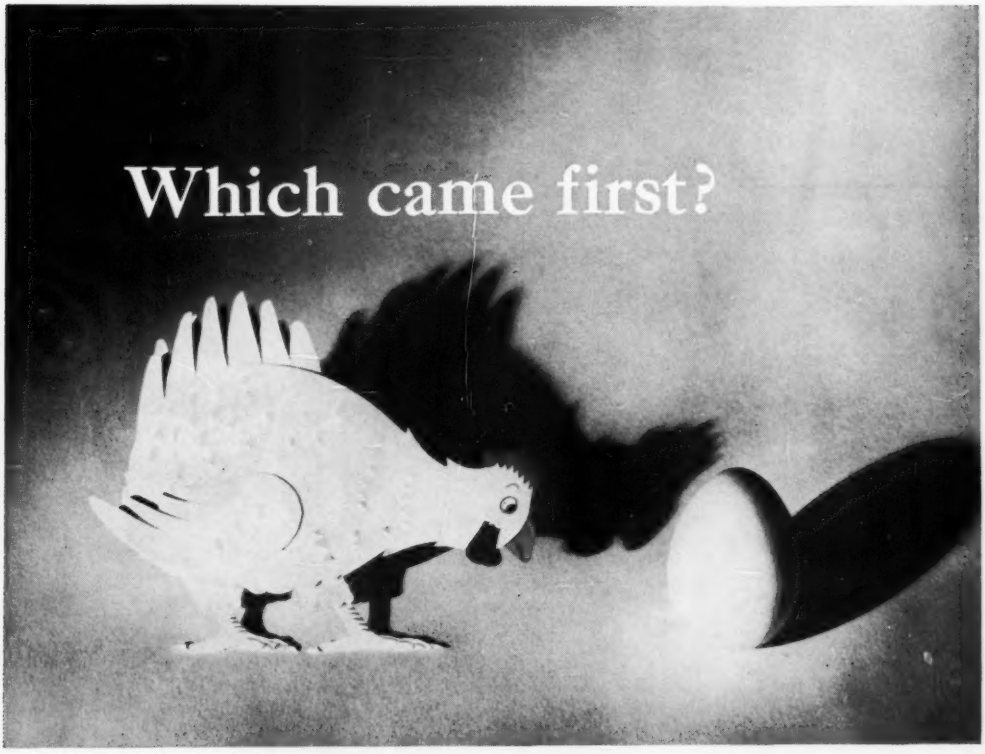

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LUBRIDERM

. . . for dry skin

You can easily judge for yourself whether Lubriderm is worth all the fuss we go to to make it. Use it yourself or have one of your patients give it a whirl. You'll find Lubriderm soothes and relieves dry, uncomfortable skin almost as fast as you can rub it in. Lubriderm never feels sticky or "smothery". Lubriderm always smooths right in without a greasy film.

We'll be glad to supply the Lubriderm, of course — just write us. If you want a stock size bottle for your own use, be sure to say so; otherwise, we'll probably just send samples.

TEXAS PHARMACAL COMPANY • SAN ANTONIO, TEXAS

EXCELLENT ANTIBIOTIC AND ANTI-INFLAMMATORY COMBINATION FOR INFLAMMATORY AND/OR INFECTIOUS DERMATOSES

NEO-MAGNACORT®

neomycin and hydrocortamate

TOPICAL OINTMENT

An extraordinary water-soluble dermatologic corticoid, MAGNACORT, combined with an outstanding topical antibiotic, neomycin, for effective control of inflammatory and/or infectious dermatoses.[1-6] Improvement or complete cure noted in 88% of a series, including many skin disorders notoriously difficult to treat.[5]

SUPPLIED: In 1/6-oz. and 1/2-oz. tubes, 0.5% neomycin sulfate and 0.5% hydrocortamate hydrochloride.

Also available: **MAGNACORT® Topical Ointment: In 1/6-oz. and 1/2-oz. tubes, 0.5% hydrocortamate hydrochloride.**

1. Howell, C. M., Jr.: Am. Pract. & Digest Treat. 8:1928, 1957.
2. Frank, L.: A.M.A. Arch. Dermat. 75:876, 1957.
3. Welsh, A. L.: Internat. Rec. Med. 169:775, 1956.
4. Robinson, H. M., Jr., et al.: Antibiotic Med. 3:461, 1956.
5. Janssens, J.: Le Scalpel 111:69, 1958.
6. Bereston, E. S.: Clinical Review 1:13, 1958.

Pfizer

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc
Brooklyn 6, New York

For the treatment of dry, scaly skin

LOWILA®
EMOLLIENT

an effective skin moisturizer

moisturizes and softens the skin

promotes moisture retention

supplements natural skin oils

restores and maintains normal skin pH

Lowila Emollient hydrates the skin . . . keeps it soft and smooth

Lowila Emollient is a new, effective skin moisturizer for the treatment of dry, scaly skin. It contains an excellent keratin-moisturizing agent Kerohydric®, a crystal-clear, dewaxed oil-soluble fraction derived from lanolin.

Lowila Emollient moisturizes the skin and promotes retention of moisture. When applied to the skin, Lowila Emollient provides a partially-occlusive "breathing" film that: (1) supplies its own water to the dehydrated keratin layer, (2) prevents excessive evaporation when the atmosphere is dry, (3) allows the skin to absorb water from an atmosphere with normal humidity.

Lowila Emollient also supplements natural skin oils, restoring the protective action of skin lipids lost through effects of water, weather and detergents. In Lowila Emollient, Kerohydric is dispersed in a lactic acid buffered emulsion that restores and maintains normal skin acidity.

LOWILA EMOLLIENT

Indications

For dryness, flaking and scaling following therapy of acute inflammation
Dermatitis of the hands ("Housewives' Eczema")
In chronic atopic dermatitis
Pruritus senilis—pruritus hiemalis
In nummular dermatitis
In psoriasis
Xerosis or asteatosis
Sunburn
Diaper rash
Chafed or chapped skin
Ichthyosis

Caution: Lowila Emollient is partially occlusive. Therefore it should not be used until the skin is free of inflammation.

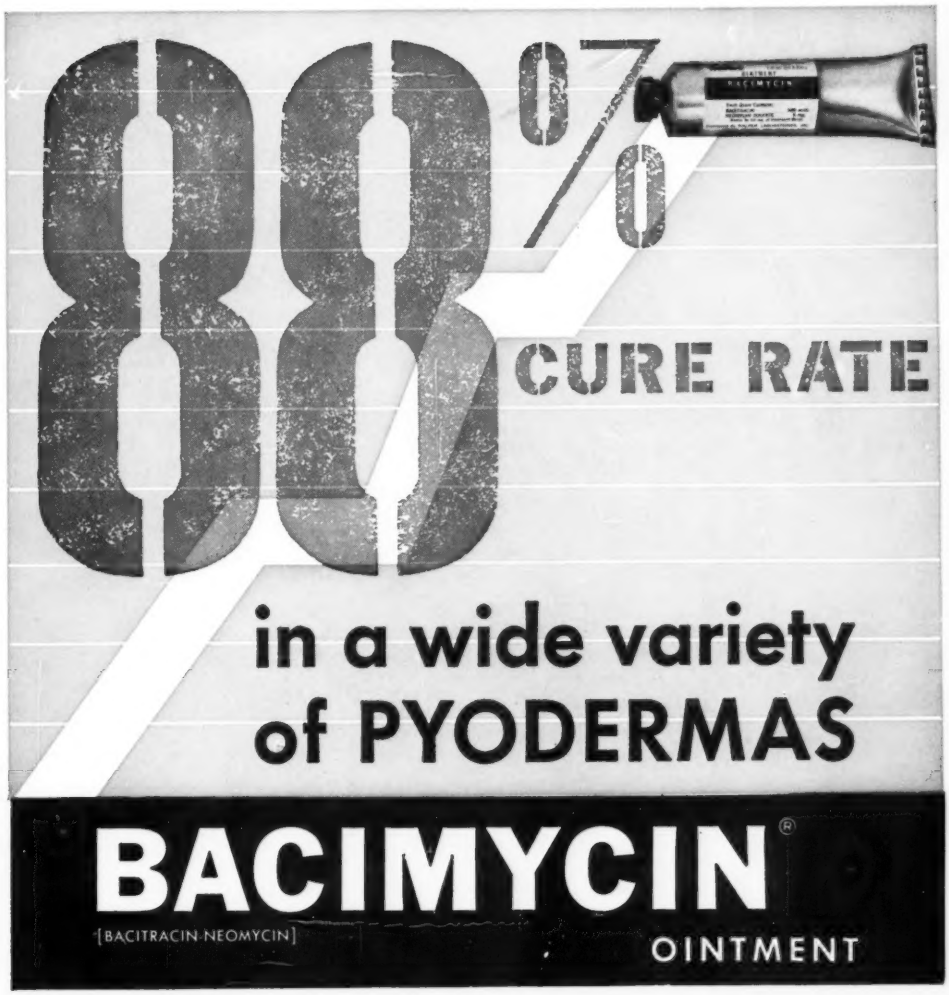
Application:

Gently rub a small amount into affected areas three or more times a day and at bedtime. Use particularly after exposure to water, soap and detergents.

Availability:

Lowila Emollient is supplied in 62.5 gram tubes.

WESTWOOD PHARMACEUTICALS
Division of Foster-Milburn Company
Buffalo 13, New York



a first choice for dual antibiotic therapy

In a recent study[1] of 53 patients with various types of pyodermas, the use of BACIMYCIN Ointment ". . . resulted in a cure rate of 88%. . . ." Impetigo, infectious eczematoid dermatitis, atopic eczema, secondary infections superimposed on dermatitis venenata, and folliculitis were among the common skin infections that showed marked improvement with BACIMYCIN therapy.

BACIMYCIN rarely produces sensitization or primary irritation.

Supplied in ½ oz. tubes for prescriptions; in 100 gm. jars for hospital use; in ⅛ oz. tubes for ophthalmic use. Also supplied as BACIMYCIN with Hydrocortisone, ⅛ oz. tube with applicator tip.

Literature and samples on request.

1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

Walker **LABORATORIES, INC.** MOUNT VERNON, NEW YORK

CULTURE MEDIA AVAILABLE

Mycosel Agar

Sabouraud's Dextrose Agar

Sabouraud's Maltose Agar

Corn Meal Agar

Potato Dextrose Agar

Sabouraud's Dextrose with Penicillin

Sabouraud's Dextrose with Streptomycin

Chlamydospore Agar

Littman's Oxgall Agar

"It is considerably cheaper to use these bottles once and discard them than to pay the labor cost of reconditioning an equal number of test tubes."

...*Practical Medical Mycology*
By J. Walter Wilson, M.D.
and Orda A. Plunkett, Ph.D.
Arch D & S 59:414, April 1949

DECEMBER 1958 (IN.

A PREFERRED METHOD for the CULTURE of FUNGI as an OFFICE PROCEDURE

WRITE FOR INFORMATIVE LITERATURE

DERM MEDICAL Sterile Glass Containers holding Sabouraud's Dextrose Agar offer a simple, accurate method for the culture of fungi pathogenic to man. When indicated for diagnosis and study of mycotic diseases, can be used as a routine office procedure. For institutional use, this method has proved both efficient and economical.

Derm Medical

Manufacturers of Culture Media in Sterile Containers

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